Supreme Court, U.S.
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IN THE SUPREME COURT OF THE UNITED STATES

Karyn Jones and Chris Jones, Petitioners, vs. The United States of America, Defendant.	Civil No. Petition for Writ Of Certiorari

On Petition For Writ of Certiorari for the Ninth Circuit

October, 1997 Term

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Questions Presented:

I. MAY THE NINTH CIRCUIT IMPOSE UPON ITS TRIAL JUDGES A MORE STRINGENT STANDARD FOR SCREENING PROFFERED SCIENTIFIC EXPERT TESTIMONY OFFERED BY PLAINTIFFS THAN THAT MANDATED BY FEDERAL EVIDENCE RULES 702 AND 403?

II. IS SCIENTIFIC EXPERT TESTIMONY PROFFERED BY A DEFENDANT SUBJECT TO THE SAME STANDARD OF SCRUTINY AS THAT PROFFERED BY A PLAINTIFF?

III. DOES A TRIAL JUDGE ABUSE HIS DISCRETION IN REJECTING AS "NOT GOOD SCIENCE" THREE PUBLISHED CONTROLLED STUDIES DOCUMENTING THE ADVERSE INTERACTION IN QUESTION SOLELY BECAUSE THE NUMBER OF SUBJECTS WERE NOT SUFFICIENT TO MAKE THE RESULTS "STATISTICALLY SIGNIFICANT"?

IV. MAY A TRIAL JUDGE RENDER THE DAUBERT TEST NUGATORY BY WITHHOLDING HIS RULINGS UNTIL HE HAS ADJUDICATED THE ISSUE OF CAUSATION FOR THE CASE AS A WHOLE AGAINST PLAINTIFF?

V. MAY THE NINTH CIRCUIT REFUSE TO REVIEW AND THEREBY GRANT UNFETTERED DISCRETION TO A TRIAL JUDGE'S "DAUBERT TEST" RULINGS IF HE HAS SIMULTANEOUSLY ADJUDICATED THE ISSUE OF CAUSATION FOR THE CASE AS A WHOLE AGAINST THE PLAINTIFF AND THEREBY RENDERED MOOT THE RELEVANCY OF THE PLAINTIFFS' EXPERT TESTIMONY?

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LIST OF PARTIES

Petitioners in this Court (Plaintiffs in the District Court and Appellants in the Court of Appeals) are Karyn Jones and Chris Jones. Respondent in this Court (Defendant in the District Court and Appellee in the Court of Appeals) is the United States of America.

OPINIONS BELOW

The opinion of the District Court is reported at 933 F.Supp 894 and appears at P.C.A[1].1-22. The opinion of the Court of Appeals is reported at 127 F.3d 1154 and appears at P.C.A 23-30.

JURISDICTION

The Memorandum of Decision of the District Court was entered on July 3, 1996. P.C.A.22. The Judgment of the Court of Appeals was entered on October 28, 1997. P.C.A.23. The Petition for Rehearing en banc was denied on January 9, 1998. P.C.A.31.

This Court has jurisdiction pursuant to 28 U.S.C. §1254.

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[1]References to P.C.A. are to Appendix to Petition for Certiorari.

RULES INVOLVED

Fed. Ev. Rule 104 (a) Questions of admissibility generally. Preliminary questions concerning the qualifications of a person to be a witness, the existence of a privilege, or the admissibility of evidence shall be determined by the court, subject to the provisions of subdivision (b). In making its determination it is not bound by the rules of evidence except those with respect to privileges.

Fed. Ev. Rule 403. Exclusion of Relevant Evidence on Grounds of Prejudice, Confusion, or Waste of time. Although relevant, evidence may be excluded if its probative value is substantially outweighed by the danger of unfair prejudice, confusion of the issues, or misleading the jury, or by considerations of undue delay, waste of time, or needless presentation of cumulative evidence.

Fed. Ev. Rule 702. Testimony by Experts. If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise.

Fed. Ev. Rule 703. Basis of Opinion by Experts. The facts or data in the particular case upon which an expert bases an opinion or inference may be those perceived by or

made known to the expert at or before the hearing. If of a type reasonably relied upon by experts in the particular field in forming opinions or inferences upon the subject, the facts or data need not be admissible in evidence.

STATEMENT

Federal Jurisdiction in this Federal Tort claims Act case was conferred upon the court of first instance pursuant to 28 U.S.C. §1346.

In May of 1991, the defendant's dentist, Dr. Cirbus, returned from Desert Storm with what his assistants were prepared to testify, but precluded by the trial judge's ruling from doing so, was a cocaine addiction resulting in his bizarre behavior including being found alone with white powder on his face and shirt, and prescribing unneeded drugs to patients. P.C.A.65-66.

In December, 1991, the American Dental Association published in the ADA Journal an article entitled "ANTIBIOTIC INTERFERENCE WITH ORAL CONTRACEPTIVES" for the express purpose of alerting all U.S. Dentists, inter alia, that:

> "The interaction between certain antibiotics and OSC has been known for the past 20 years....All women of childbearing age should be informed of possible reduced efficacy of OSC during antibiotic therapy and advised to use additional forms of contraception during short-term antibiotic use." (Plt's Exhibit

37,12496[2], 141:02-145:20)

Dr. Scott Grace, a Board Certified general dentist with over 20 years of practice in Monterey County, California testified that from the date of its publication the above ADA directive set the standard of care for all dentists in Monterey County and the U.S.(12496,145:20).

Karyn had a history of 10+ years of success with birth control pills and clearly indicated on her dental chart that she was taking them when she reported to the Ft. Ord Army dental clinic for a sore tooth on February 7, 1992. Dr. Cirbus did not see Karyn but instructed his assistant Susan Balesteri to order Karyn to take 2000mg of Penicillin V for six days in preparation for root canal oral surgery. He did not instruct Balesteri to warn Karyn to take additional contraceptive precautions, and Balesteri' a young married woman in her latter 20's, indicated that she did not so warn Karyn because she herself was unaware of the potential danger.

Evidence in the form of expert testimony was introduced by both experts which established that post pubescent females have 28 day menstrual cycles; the period or menses begins on day one (1) of the cycle which is also the day of her LMP (first day of last menstrual period or menses); women are presumed to ovulate on the 14th day of their cycle[3]

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[2] The volumes of the Reporters transcripts are referred to by the date of the proceedings reported, e.g. 12495.

[3]Cross exam of Dr. Archer by Mr. Loftus: 121295, 1058:

women are presumed to ovulate on the 14th day of their cycle[3] and can conceive only on the day of ovulation, not on the day before or after.

The accuracy of Karyn's post pregnancy indication that her last LMP was January 27, 1992 was supported by the fact that during her January 16 checkup with an Army Ob-Gyn, who listed that she was not pregnant, she indicated her previous LMP as December 30 (exactly 28 days prior to January 27, 1992). This means that she was scheduled to ovulate on February 9, 1992 (the 14th day of her cycle) and her next menses or LMP was due to begin on February 24, 1992.

Karyn began taking 2000mg (500mg X4 per day) on February 8 (on an empty stomach as ordered).

On February 19, 1992, Dr. Cirbus' dental responsibilities with Karyn having were taken over by the

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[3]Cross exam of Dr. Archer by Mr. Loftus:
121295, 1058:

03 Q Okay. Thank you. And generally speaking, if I
04 understood your testimony correctly, experts such as yourself
05 arbitrarily ascribe a 14 day period from the LMP, that is the
06 first day of the last menstrual period. 14 days thereafter is
07 generally considered the day of ovulation?
08 A Yes, and we don't do that arbitrarily. We do that
09 based on some investigation, and so the usual duration of
10 follicular maturation with the beginning point of the first day
11 of menstrual is 14 plus or minus two days.

head of the Department, Dr. Caples, who promptly (but too late) warned Karyn to take additional contraceptive measures when taking penicillin with her birth control pills. In addition on February 19 Dr. Caples' staff administered an Icon II urine pregnancy test to Karyn which came back positive.

The package insert for the Icon II urine pregnancy test specifically stated that it could show positive "4-5 days before the first missed menses" and which in Karyn's case would have allowed for a February 8 or 9 conception to be evidenced by the February 19 test (i.e. February 24, her next due and first missed menses, minus 5 days = February 19).

In addition, Karyn had three post pregnancy ultrasounds taken and all of the measurements (P.C.A.68-69) with the exception of the first single "Biparietal diameter" measurement (which both the physician who designed the very ultrasound used as well the physician who applied and took the ultrasound reading indicated should not be relied upon) were consistent with her having conceived on February 9, 1992[4]. In addition the baby's birth date of October 2, 1992

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[4] Both Karyn's and the Government's experts (with the exception of defendant's Dr. Roy) along with ALL of the published studies on the subject agreed that determining date of conception is relatively simple. You simply find the first day of bleeding of a female's LMP or "last menstrual period" and add 14 days (allowing a 1 or 2 days for individual variation) and you have the date of conception. "Gestational age" or "menstrual age" is generally dated from

was consistent with an early term baby conceived on February 9, 1992.

As was laboriously pointed out to the trial judge during final argument.(62696,28:15-56:12), however, Dr. Hadlock who designed the very BPD measurement relied upon by defense experts, in a published article specifically which the defendant acknowledged as authoritative, cautioned physicians to ignore such a BPD measurement. (Because the "Cephalic index" readout was 86% which was greater than his 83% limit. Plt's EX. 157:91-93.) In such a case, Dr. Hadlock recommended the use of the head circumference measurement instead of the BPD and which indicated 14wks3days. (which would (given the range of error of +/- 7 days) allow for the LMP of Jan 27 and conception of Feb 9.)

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the first day of a females LMP, however, because there is strong "good science" evidence to support the expectation that a female will ovulate on the 14th day of her menstrual cycle. Fetal Cephalometry, Michael John Hughey, D-13.108, p75 (offered and relied on by Dr. Roy (121495,82:1-84:22) (Karyn's LMP was January 27, 1992 which would place her ovulation at February 9), 14 days is added to the LMP to arrive at the estimated date of conception. (Plt's Exh. 157, Ultrasonography in Obstetrics and Gynecology, 3rd Ed., Peter W. Callen, M.D.,1994 W.B.Saunders Company, Chapter 7:Ultrasound Determination of Menstrual Age, Frank P. Hadlock, M.D., p1, first Par; Dr. Roy 121495, 84:1-87:11).

The trial judge (having sustained defendant's objection to Plaintiff's calling a board certified radiologist who would have also testified that in his opinion Karyn conceived on February 9), however, rejected the ultrasound evidence as "inconclusive"[5]. Instead he adopted the solitary (there were four Ob-Gyn's who testified in the case) testimony of defendant's Dr. Roy, sans a scintilla of evidence of a "good science" basis[6], that at least 13 to 14 days post conception must expire before the Icon II urine pregnancy test can show positive and concluded that:

> If a pregnancy test administered on February 19 was positive, Karyn must have conceived, at the latest, on February 6 or 7. P.C.A:21.

In support of the above the trial judge's DECISION simply quotes from the unsupported testimony of the defendant's Dr. Roy. P.C. A:20) However, it was repeatedly

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[5]After examining these ultrasounds in detail, the Court finds them to be "inconclusive" in determining the date of Abbigayle's conception....P.C. A:21, fn.16.

[6]The only item offered in support of Dr. Roy's testimony was a paper that he had co-authored, (and which the defendant failed to include within its 8 volumes of Supplemental Excerpts of Record filed with the Court of Appeals in this case) but which reflected no testing that he had done and did not refer to his "13-14" post conception lapse of time requirement, but only appeared to be a summary of various pregnancy tests' package insert information.

pointed out to the court that Dr. Roy's above testimony was in direct conflict with the Icon II urine pregnancy test which indicated that it could show positive "4-5 days before the first missed menses".

Since it was undisputed that a typical female ovulates on the 14th day of her 28 day cycle, and can conceive only on the day that she ovulates, her first missed menses of LMP will occur on the 15th day after ovulation. Thus, for Dr. Roy's opinion and the Court's DECISION to be "consistent" the package insert, the latter would have to be changed from "4-5" to "1-2" days before the first missed menses.

In addition, the trial judge adopted the following affirmative defenses based solely upon defendant's expert testimony and with no indication of having subjected them to Daubert screening:

That Karyn conceived no later than February 6 or 7 and before taking the Penicillin on February 8, because even if the Penicillin had knocked out the estrogen component of her Wyeth Ayerst Triphasil 28 combination birth control pill, the progestin would have provided sufficient contraception action by itself.

And, Karyn conceived no later than February 6 or 7 and before taking the Penicillin because having taken birth control pills since February 2 she could not have ovulated on February 8 or 9 because her follicle development would have been impaired.

At this point the undersigned feels in danger of appearing to patronize the Court with the following

observations, however, since this is an appeal from a Ninth Circuit opinion which found the above trial judge's findings of scientific fact to be "not clearly erroneous" and dispositive of the case, we must, respectfully, proceed.

In affirming the above "dispositive" findings of fact the Court of Appeals ignored:

1. The fact that they applied, a fortiori, to his conclusion that Karyn conceived no later than February 6 or 7;

2. Karyn's ovulation due date of February 9;

3. Her 10+ year successful history of taking birth control pills prior to this solitary failure;

4. The "good science" evidence introduced by defendant which established a five fold increase (not just "X2") in contraceptive failure for progestin only pill users as opposed to estrogen-progestin combination pill users;

5. Defendant's Dr. Archer's "good science" study which showed that all women on all forms of birth control pill demonstrate follicle development similar to women not on the pill; P.C.A., 70-71.

6. Defendant's "good science" study which concluded that ovulation could occur rapidly upon cessation of oral estrogen; P.C.A.,70-71.

7. The birth control pill's package insert which cautions the use of alternate means of contraception if two consecutive pills are missed.

8. The Package Insert for Penicillin V, approved by the FDA, and issued in 1987 stated under **Drug Interactions:**

Oral Contraceptives--"Oral contraceptives may be less effective and increased breakthrough bleeding may occur."

9. Defendant's Dr. Judith Jones testimony regarding the FDA's "combination drug policy". P.C.A. 72.

10. In addition the American Medical Association as well as other highly respected treatises on Drug Evaluations relied upon by drug prescribing health care specialists warned of the danger of the interaction. P.C.A., 39-40.

MECHANISM OF INJURY

Further, there was substantial evidence of general acceptance of the mechanism by which the adverse interaction between antibiotics and birth control pills occurs.

A letter from the very manufacturer of the oral contraceptives which failed Plaintiff Karyn Jones in this case, Wyeth Ayrst, to her Ob-Gyn expert, Dr. William Hinderstein sets forth an excellent summary of the "consensus of opinion" as to both the occurrence and mechanism for the adverse interaction. In essence the evidence established that the estrogen component of a combination estrogen-progestin birth control pill (the typical pill) would be excreted after the "first pass" through the female's bowels were it not for the action of certain "friendly microbial" or gut flora that are naturally found in the human stomach and which aid in the digestive process. As Dr. Hinderstein explained (P.C.A.33-38) 40% of the estrogen is "passed" or excreted after the first 12 hour pass though the females bowels. 60% is "bound" by reason of the action of the above gut flora so that it

recirculates through the system. Penicillin was shown by Karyn's Dr. Arthur Harralson based upon a reputable study to be the "microbial of choice" for killing the gut bacteria in question.

Dr. Hinderstein testified:

Penicillin is a bactericidal drug, and "cidal" means killer....

THE COURT: There's good guys and bad guys?

THE WITNESS: That's true. That's the problem of antibiotics, they can kill good guys, like the clostridium in the bowel. A cidal drug, it kills the bacteria, it doesn't just slow them down, and it kills them fast. P.C.A.35.

Defendant's Primary Research Expert, Dr. Archer, Concurred That Three Controlled Studies Relied Upon by Karyn's Experts Were "Good Science" And Supported Their Opinions That an Adverse Interaction Between Antibiotics And Birth Control Pills Can Occur in Some Women. P.C.A. 58-62.

The Swenson controlled study concluded:

> **These studies suggest that metabolism of exogenous estrogen contraceptives is influenced by tetracycline and ampicillin, probably by inhibiting bacteria that deconjugate estrogen**. In some women (3/5 in our small series), these antibiotics produced rapid elimination of EE2 and a shift toward increased fecal and decreased urinary excretion. P.C.A. 41.

The Shenfield & Griffin controlled study concluded:

> This individual had repeated breakthrough bleeding when taking courses of antibiotics and it appears that his was probably due to lower concentrations of ethinylestradiol when on the combination of drugs. P.C.A.42-45.

The trial Judge's DECISION[7] does not mention the Back study's bold faced conclusion #3 on the first page of the published report of his study (page 43, Plt's Exhibit 56):

> "We conclude that **most** patients taking oral contraceptive steroids do not need to take alternative contraceptive precautions while taking ampicillin."

Further, the trial judge does not mention Back's explanation for his use of the above word "most" on the last page, page 47:

> "In only two of our patients (Patients 1 and 3) was there a suggestion of an effect of ampicillin on the plasma concentration of ethinyloestradiol and although FSH concentrations in plasma rose in one of these patients, there were no changes in the plasma progesterone concentration and thus no evidence that ovulation had taken place. It is possible that this interaction may occur in occasional women since there

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[7]DECISION refers to the trial judge's Memorandum of Decision found at P.C.A.1.

> appear to be marked variations among individuals in the concentrations of EE excreted in bile. (Cargill et al., 1969). A negative result may have been seen since it is possible that the patients and subjects did not take their ampicillin as prescribed..."

Defendant's primary expert on scientific research, Dr. David Archer, admitted from the witness stand that each of the above three published articles represented controlled scientific tests which each supported Karyn's expert's opinions as to the occurrence of the adverse interaction between antibiotics and birth control pills.(P.C.A. 58-62)

THE OPINIONS & NINTH CIRCUIT "GUIDELINES"

The Trial Judge's Memorandum of Decision appealed from in this case cites the following guideline set forth in the Ninth Circuit's DaubertII[8] decision:

> Federal judges must therefore exclude proffered scientific evidence under Rules 702 and 403 unless they are convinced that it speaks clearly and directly to an issue in dispute in the case, and that it will not mislead the jury. DaubertII at 1321,fn.17. (P.C.A.:13)

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[8]"Daubert I" will be used herein to refer to Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993) "DaubertII" will refer herein to Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311 (9th Cir. 1995)

The Ninth Circuit's DaubertII Court, after concluding that on remand the Daubert Plaintiffs' might be able to satisfy the "good science" prong of the Daubert test, rather than simply limiting its "fit" prong inquiry to whether their experts testimony would advance Plaintiffs' case on the issue of causation, set about to determine whether the advancement would be sufficient to permit the Plaintiffs to prevail on that issue for the case as a whole.

Toward that end it proceeded to immediately ignore its above rigid screening rule when it came to defendant's proffered SET[9] by adopting a dispositive finding of scientific fact (viz., that nobody knew how teratogens caused birth defects) in favor of the defense (which did not appear in the trial judge's opinion[10]) and without citation to a scintilla of

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[9]SET refers to "scientific expert testimony".

[10]The following trial court dicta, rather than reflecting its own weighing of the evidence and factual conclusion seems to demonstrate a new post Daubert Test tendency of Courts to simply cite conclusions of fact made by other courts based upon different evidentiary records as if they were statements of law having binding precedential authority, viz.:

> Absent a scientific understanding of the cause of the birth defects at issue in Bendectin cases, causation may be shown only through reliance upon epidemiological evidence. *Daubert Vs. Merrell Dow Pharmaceuticals, Inc* 727 F. Supp. 570, 572 (USDC, SDCAL, 1989)

good science reliability to support it.[11]Certainly the parties had not stipulated to the Court's scientific conclusion, nor did it qualify under DaubertI for Judicial notice:

> Scientific theories that are so firmly established as to have obtained status of scientific law, such as laws of thermodynamics, properly are subject to judicial notice.*DaubertI,supra, fn.11.*

Next, the Ninth Circuit's DaubertII Court took its scientific conclusion that no one knew the cause of birth defects and used it to further determine as a matter of law that Plaintiffs could only carry their burden of proof on the issue of causation through statistical proof, viz., that those who took Bendectin had an increased exposure to birth defects of at least double ("2") those who did not. Finally, rather than staying within the Daubert test framework, it undertook to essentially adjudicate the issue of causation for the case as a whole against Plaintiffs (i.e. concluding that Plaintiffs could not make a prima facie case on the issue of causation by way of statistical proof) as its way of mooting the "fit" prong of the Daubert test by essentially showing that Plaintiffs'

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[11]"But scientists simply do not know how teratogens (chemicals known to cause limb reduction defects) do their damage: They cannot reconstruct the biological chain of events that leads from an expectant mother's ingestion of a teratogenic substance to the stunted development of a baby's limbs. Nor do they know [*1314] what it is about teratogens that causes them to have this effect". Daubert2, at 1313.

scientific expert testimony evidence was not sufficient to allow them to prevail on the issue of causation for the case as a whole.

In his handling of the instant case the Trial Judge, like another NDCal judge before him[12], applied the above DaubertII "guidelines". Staying within the Daubert Test framework he refused to promptly rule on the admissibility vel non of the parties respective SET but took his rulings under advisement and thereby forced the parties to conditionally put on all of their evidence. Then after both parties had rested he proceeded to exclude all of Plaintiffs' SET while simultaneously adjudicating the issue of causation for the case as a whole against them, thereby attempting to moot rather than address the "fit" or relevancy prong of the test, e.g.:

After considering the entire record, the Court finds

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[12] The term "causation" has two meanings here, both of which must be examined under Daubert. The first is general causation; that is in this case, whether halothane can cause chronic active hepatitis. The second is specific causation; that is in this case, if halothane can cause active hepatitis, whether it did cause plaintiff's chronic active hepatitis (Casey, supra, 1382)... because specific causation is a vital step in the required chain of legal causation here, and because of the attention given to the subject by the Supreme Court and the Ninth Circuit, this court has also examined plaintiff's evidence of specific causation."(Emphasis supplied) (*Casey v. Ohio Med. Prods., 877 F. Supp. 1380, 1386 (NDCal, March 1995)*

that Plaintiffs' evidence of causation does not meet the Daubert standard for admissibility in federal court. Furthermore, even if this evidence were admissible, the Court finds that Plaintiffs' have failed to satisfy their burden of proof on several elements of their case. P.C.A.,1.

The Judge applied DaubertII's overly rigid Daubert test's "good science" prong screening to exclude all of Plaintiffs' SET

The trial judge repeatedly expressly stated on the record that he viewed Plaintiffs' evidence as part of a "health scare" conspiracy sweeping the nation and that it was part of his duty to oppose it. P.C.A.46-47.

He also revealed on the record that he was relying upon evidence that he was obtaining on his own outside the courtroom proceedings. P.C.A. 48.

While expressly acknowledging two published controlled studies which demonstrated an adverse interaction between antibiotics and birth control pills the judge flatly rejected them solely because the number of subjects were not large enough to make their results "statistically significant"and because they didn't test for other factors. In addition, the Judge ignored language in a third published controlled study, *Back '82*, in which the author clearly acknowledged the occurrence of the adverse interaction in 2 of his 11 subjects. (See pp 12-14, supra.)

> In other words, Plaintiffs' witnesses took data from articles that found no statistically significant correlation between antibiotic use and increased failure of oral contraceptives, and used the data to reach a conclusion contrary to the articles' own authors. This tactic does not qualify as good science. (P.C.A:8)
>
> In sum, Plaintiffs' witnesses did not rely on a single controlled study that showed a statistically significant correlation between antibiotic use an decreased effectiveness of oral contraceptives. Consequently, the Court finds that Plaintiffs' evidence does not satisfy the first prong of the Daubert standard.(P.C.A.,12)
>
> Given that over 14 million women in the United States are currently using oral contraceptives, and an unknown number of them are prescribed antibiotics from time to time, Plaintiffs' reliance on studies involving only a handful of women is clearly

With respect to the trial judge's criticism of the above studies on the grounds that they did not test for ovulation, the evidence was that such a test would not have been significant particularly for women such as Karyn on taking low dose estrogen birth control pills such as Wyeth Ayerst's Triphasil 28 where defendant's Dr. Archer's own study showed that it is not uncommon to have females ovulate while on the pill. P.C.A. 70-72. In such cases the estrogen in the pill is thought

to accomplish contraception by one of two other methods. P.C.A.37.

Further, the evidence was that no study is perfect and all studies are subject to second guessing and suggestions that different factors might have been considered.

Modern Epidemiology by Kenneth Rothman, 1986, (Plt's Exhibits 160, 161) was unequivocally recognized by both defendant's self-styled epidemiologist, Drs. Jones (597:19) and Grimes (1282:1-1284:23), as a "good epidemiology book" and deserving of respect among their peers. Rothman criticized those who come up with some slight change or modification to question the quality of a studies results. P.C.A. 63.

There was absolutely no evidence in the record that "statistical significance" is a prerequisite to reliability in scientific research. In fact Rothman, supra, expressly rejected the concept of "statistical significance" in attempting to test the significance between exposure and disease. P.C.A. 63-64.

Finally, the trial judge totally ignored Plaintiffs' substantial good science evidence of the very mechanism by which antibiotics interfere with the efficacy of birth control pills. The Swenson as well as the Shenfield & Griffin articles (P.C.A., 39-43), as well as the American Medical Association and other highly respected publications on drug interactions all concur that the mechanism of the harm is caused by the antibiotic killing off the natural flora needed to assist in the insulating and entero-hepatic recirculation of over 50% of the exogenous estrogen provided by the pill so that it will not all

be excreted at the end of the "first pass" at approximately 12 hours, and leave the female defenseless for the remaining 12 hours. (Penicillin having been shown by another study, Moellering to be the microbial of choice for killing this type of flora or bacteria.)

The trial judge, nevertheless determined that Plaintiffs could only meet their burden of proof on the issue of causation statistically as stated in DabuertII:

> Under Daubert, Plaintiffs could carry this burden if they could show that such an interaction occurs at more than double the rate of the known failure rate for oral contraceptives alone. 43 F.2d at 1320 ("plaintiffs must establish not just that their mothers' ingestion of Bendectin(sic) increased somewhat the likelihood of birth defects, but that it more than doubled it") (P.C.A.,15)

However, Plaintiffs should have been able to survive the above statistical requirement due to evidence introduced by defense experts which, they testified, was amply supported by good science, namely, the Trussell & Kost, study displayed on the first page of the complex package insert and approved by the FDA, namely, 0.1% for consistent users of combined estrogen-progestin pills, 0.5% for progestin only pills.

The Government's expert, Dr. David Archer's sworn testimony revealed a rigorous maximum failure rate that a birth control pill manufacturer must establish before it can obtain FDA approval to be marketed in the U.S.: "If you try to get an oral contraceptive on the U.S. market, you have to

show that it has less than 1 pregnancy per 1,000 women using it for one year".(121195, 909:10)

Further, he revealed that drug manufacturing companies pay for 99% of all drug studies. (Thereby explaining the absence of large scale epidemiological studies and why drug company experts who testified for the defendant in this case said there is "no interest" in conducting further studies which might result in losing FDA approval to market in the lucrative birth control pill market.)

Granted, the Trussell table does refer to a "Typical" failure rate of "3%", but this does not apply to Karyn (who's testimony indicated that she religiously and successfully took her pills over a 10 year period 12495,22-25) because the author (by footnote) expressly expands the "3%" figure to includes those who DO NOT use the pills "consistently and correctly". Those who use the pills "consistently and correctly" are expressly included within the 0.1% expected failure rate.

Citing only the trial Judge's own DECISION as the sole basis for affirming on the grounds that they were "not clearly erroneous", the Court of Appeals declined to address any above issues raised on the appeal.

ARGUMENT:

The U.S. Supreme Court's recent GENERAL ELECTRIC COMPANY v. JOINER decision (118 S.Ct. 519, Dec.1997) established the rule that Circuit Courts of Appeal should apply an abuse of discretion standard in reviewing District Court's Daubert test rulings excluding or admitting evidence. (Since the instant Ninth Circuit ruling denying Plaintiffs petition for rehearing en banc was issued on January 9 it may not have had the time to absorb the wisdom of Joiner, supra)

For practical purposes, the *Joiner* decision essentially placed a cap on the liberal policy of a Circuit in requiring the admission of proffered scientific expert testimony (hereinafter referred to as SET).

The instant case provides the Court with an important opportunity to place a cap on the policy of the Ninth Circuit in excluding Plaintiffs SET only and in admitting Defendant's SET only.

The instant Ninth Circuit Court of Appeals opinion appealed from completes an unusually erroneous misapplication of the DabuertI case law so as to essentially render the Daubert test nugatory in the Ninth Circuit by establishing the binding precedent that if a trial judge follows the "guidelines" and example set by the Ninth Circuit in DaubertII, his Daubert test rulings will not be subjected to any review whatsoever on appeal even though they may be the result of a gross abuse of discretion.

In addition by failing to first take up the Judge's

critical evidentiary rulings before it addressed the issue of whether his findings of fact were, vel non, "clearly erroneous" the Court of Appeals permitted the Judge to violate substantive controlling California law which requires the trier of fact to consider and weigh all admissible (but not inadmissible) evidence before arriving at his findings of fact.[1]

The typical savvy U.S. District Judge who reads the instant trial judge's and Court of Appeals opinions will quickly learn that if he intentionally fails to promptly issue his Daubert screening rulings on Plaintiffs' proffered scientific expert witness testimony, but takes them under advisement thereby forcing the parties to put on all of their evidence he can escape all accountability for his errors if simultaneous with his Daubert test rulings excluding all Plaintiffs' SET and adopting all Defendant's SET he makes dispositive findings of

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[1] California Jury instruction BAJI 2.60 provides in part: "You should consider all of the evidence bearing upon every issue regardless of who produced it."

If the Judge has improperly excluded Plaintiffs' core evidence on the issue of causation, then he violates this basic rule applicable to his role as the trier of fact when he proceeds to adopt dispositive affirmative defenses on the causation issue without the benefit of Plaintiffs' valid and admissible evidence. Likewise, when he improperly admits defendant's expert testimony which does not qualify under the most rudimentary Daubert Test, he likewise is considering inadmissible evidence in reaching his findings of fact.

fact in favor of the defense on the issue of causation.

Further, a District Judge presiding over future Jury trials who desires to see a particular party prevail, can withhold his Daubert test screening rulings until the Jury has heard all of the scientific expert testimony and rendered their judgment. If the judgment is to the Judge's liking he can then rule that the prevailing parties' SET met the Daubert standard, however, if not, he could retroactively (like the trial judge in the instant bench trial did) exclude the prevailing parties SET and then either sustain a Rule 52 (c) motion by reason of that parties resulting inability to make a prima facie case on the issue of causation, or direct the verdict against the less favored party.

DaubertI was expressly intended by the U.S. Supreme Court to liberalize the U.S. District Courts approach to the admission of scientific expert testimony by doing away with the Fry general acceptance requirement and requiring judge's to apply Federal Rules of Evidence Rules 702, 703.

However, in its excitement at seizing the opportunity to trump the U.S. Supreme Court's remand it respectfully submitted that the Ninth Circuit's DaubertII Court may have taken one "deep breath" too many as it has established some erroneous guidelines which in this case has lead to a far more restrictive rule and, for all practical purposes, rendered the Daubert hearing nugatory in the Ninth Circuit.

As it now stands this case stands for the proposition that a trial judge may commit the most glaring abuse of discretion in excluding all of Plaintiffs' scientific expert

testimony and in admitting defendants with complete impunity to any scrutiny whatsoever on appeal as long as he improperly withholds his rulings until all of the evidence has been offered and then couples his rulings with dispositive findings of fact on the issue of causation.

In the latter instance, this case stands for the proposition that the Ninth Circuit Court of Appeals will not address the critical issues raised as to the judges errors in his evidentiary rulings, but narrow its review solely to the question of wether the judge's dispositive findings "are not clearly erroneous".

CONCLUSION:

In *Joiner*, supra, this Honorable Court stated:

> We hold that the Court of Appeals erred in its review of the exclusion of Joiner's experts' testimony. In applying an overly "stringent" review to that ruling, it failed to give the trial court the deference that is the hallmark of abuse of discretion review.

Applying the same type of reasoning to the instant case, the Court might be inclined to hold that the Ninth Circuit's extrapolation of DaubertI dicta has created an affirmative duty of strict scrutiny for District Judges beyond that established by the Federal Rules of Evidence or by DaubertI.

DaubertII was cited as the guiding principle for the

instant District Judge as he proudly and repeatedly expressed his antagonism on the record toward the "health scare industry" (into which grouping he obviously placed Karyn's experts testimony and their Daubert test showing).

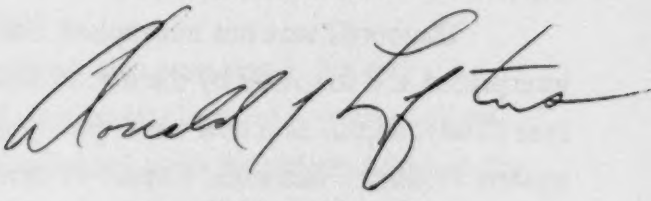
DaubertII was not misapplied, but was correctly interpreted and followed by the instant trial judge and others (see *Casey,* supra) as a new harsh policy of the Ninth Circuit against Plaintiffs' Scientific Expert Testimony only and giving them carte blanche leave to review and adjudicate the issue of causation for the case as a whole as part of the Daubert hearing process.

Applying the above reasoning of the U.S. Supreme Court in the recent Joiner, supra, decision, it should rightfully be concluded that this new and overly "stringent" screening obligation imposed by DaubertII upon the trial judge likewise fails "to give the trial court the deference that is the hallmark of abuse of discretion review".

By refusing to review the trial judge's Daubert Test rulings which were the central issues briefed and argued by the parties in this case the Ninth Circuit now establishes a new precedent which: is in direct conflict with the U.S. Supreme Court's *DaubertI* and *Joiner* decisions, renders the Daubert test nugatory, and should not be permitted to remain as viable appellate case precedent binding upon all Ninth Circuit District Judges.

Dated: April 8, 1998

Respectfully Submitted:



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UNITED STATES DISTRCIT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

Karyn Jones and Chris Jones, CIVIL NO. 93-20137
SW
Plaintiffs

Memorandum of Decision

vs.
United States of America,
Defendant.,

Plaintiffs Chris and Karyn Jones brought this wrongful birth action against Defendant United states under the Federal Tort Claims Act, 28 U.S.C. §§ 2671 et seq., to recover costs and damages associated with the birth and upbringing of their daughter Abbigayle. According to Plaintiffs, the United States is responsible for Karyn's pregnancy because U.S. Army doctors negligently failed to warn Karyn that the penicillin they prescribed for her could interfere with the effectiveness of her birth control pills.

The Court bifurcated the case and conducted a two-week bench trial on the issue of liability. After considering the entire record, the Court finds that Plaintiffs' evidence of causation does not meet the Daubert standard for admissibility in federal court. Furthermore, even if this evidence were admissible, the Court finds that Plaintiffs' have failed to satisfy their burden of proof on several elements of

their case. This memorandum constitutes the Court's findings of fact and conclusions of law as required by Fed. R. Civ. P. 52 (a).

FACTS

In early 1992,[1] at the time of the events leading to this lawsuit, Karyn and Chris Jones were married and living together at Fort Ord, California. Chris was an active-duty sergeant in the U.S. Army. Trial Transcript ("TR.) Vol. 1, at 22, 27.

On January 16, Karyn went to an Army gynecologist, Dr. James Murphy, M.D., for an annual examination and to obtain a prescription for birth control pills. Dr. Murphy conducted a pap smear which showed that Karyn was not pregnant. Dr. Murphy also prescribed Triphasil-28 birth control pills, but he did not warn Karyn of the possibility that antibiotics could interfere with the effectiveness of her birth control pills. Tr., Vol.1, at 23.

Karyn began taking her birth control pills on February 2. Tr., vol.1,at 24. During this time, Karyn and her husband had sexual intercourse an average of once per night. Tr., vol. 1, at 34.

On February 7, Karyn went to the Army dental clinic at Fort Ord complaining of a toothache. The dental clinic referred Karyn to the oral surgery unit at Silas B. Hays Hospital, where oral surgeon Dr. Mark Cerbus, D.D.S. examined Karyn and determined that she needed oral surgery.

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[1] Unless otherwise stated, all dates in this Order refer to 1992.

To assure that no infection would be present at the time of surgery, Dr. Cerbus prescribed Penicillin-VK, an antibiotic, to be taken four times a day for six days. Karyn's medical chart indicated that she was taking birth control pills, but neither Dr. Cerbus nor his dental hygienist Susan Balistreri warned Karyn that the Penicillin-VK might interfere with the effectiveness of her birth control pills. Tr., vol, 1, at 27-30.

Karyn took four antibiotics per day on February 8 and 9, three pills per day on February 10 and 11, two pills on February 12 and one pill on February 13. Tr., Vol.1, at 32-33.

On February 19, Karyn returned to the dental clinic to have some lab work done in preparation for surgery, including a routine pregnancy test. She saw another oral surgeon, Dr. Caples, during this visit. Dr. Caples warned Karyn that antibiotics could reduce the effectiveness of her birth control pills. Tr., vol. 1, at 53-54.

The next day, Karyn was informed that her pregnancy test was positive. A second pregnancy test performed on February 21 was also positive. Tr., vol. 1, at 54-55.

After discovering that she was pregnant, Karyn discussed her options with her husband. Although neither Chris or Karyn wanted more children, and Karyn had had an abortion on a prior occasion, the Jones decided to continue Karyn's pregnancy to term. Tr., vol. 1, at 56-57, 101-102.

Karyn gave birth to Abbigayle, a healthy baby girl, on October 17. Tr., vol. 1, at 57. since her birth, Abbigayle has had no significant health problems and has lived primarily with her grandparents in Mississippi. Abbigayle has only sporadic

contact with her biological parents.

On August 11, Plaintiffs filed a Standard Form 95 administrative claim against their Army doctors for malpractice and wrongful life. The Army denied Plaintiffs' administrative claim on April 22, 1993. Plaintiffs thereafter filed this suit in federal court.

ANALYSIS

The Court bifurcated this case for purposes of trial. The sole issue in the first phase of the case is liability: whether the United States is liable for the costs attributable to Karyn's pregnancy and raising Abbigayle.

I. Admissibility of Plaintiffs' Scientific Evidence Under Daubert

As a threshold matter, the Court must determine whether Plaintiffs' scientific evidence regarding the supposed interaction between antibiotics and oral contraceptives satisfies the standard developed by the Supreme Court in Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993), and explained further upon remand by (to) the Ninth Circuit in Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311 (9th Cir. 1995), cert. denied, 116 S.Ct. 189 (1995). Under the Daubert standard, medical evidence is admissible in federal court only if it both: (1) reflects "scientific knowledge"; and (2) is "relevant to the task at hand." Daubert, 509 U.S. at 597; Daubert, 43 F.3d at 1315.

A. Scientific Knowledge

To qualify as scientific knowledge, an inference or assertion does not have to be proven as an "absolute certainty," but it must be "derived by the scientific method" and "based on scientifically valid principles." Daubert, 509 U.S. at 590; Daubert, 43 F.3d at 1316. Factors that may be relevant in determining whether evidence is based on scientific knowledge are: (1) whether the theory employed by the expert is generally accepted in the scientific community; (2) whether it has been subjected to peer review and publication; (3) whether it can be and has been tested; and (4) whether the known or potential rate of error is acceptable. Daubert, 509 U.S. 593-94; Daubert, 43 F.3d at 1316-17.

Testimony that grows naturally out of an expert's own independent research is generally more reliable than opinions an expert has developed for the sole purpose of testifying in court. Daubert, 43 F.2d at 1317. This is the case because experts whose findings flow from their own research are less likely to be biased by the promise of monetary compensation for their testimony. Id. Moreover, because there are likely to be very few experts researching the specific subject that is at issue at trial, testimony by those experts provides a natural constraint on the parties' abilities to "shop for experts" who will support their desired interpretation of the evidence. Id.

If an expert does not testify based on independent research, the party offering such testimony must come forward with other "objective, verifiable evidence" that is based on "scientifically valid principles." Id. at 1318. Peer

review and publication are valid principles." Id. at 1318. Peer review and publication are the most important means of ensuring that an expert's methodology is sound. Id.

In this case, Plaintiffs presented two witnesses to testify about the supposed interaction between Penicillin-VK and Triphasil-28 birth control pills: Dr. Hinderstein, M.D.[2] and Dr. Harralson, Pharm.D.[3] Neither of these witnesses have done any independent research in the area of antibiotic/oral contraceptive interaction. Tr.,vol.2, at 223-224, vol. 4, at 620. Therefore, the Court's inquiry here is limited to whether each testified based upon objective, verifiable evidence that was derived from scientifically valid principles. In essence, the Court must determine whether the articles upon which the witnesses based their opinions are supported by good science.

After carefully considering Dr. Hinderstein's and Dr.

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[2]Dr. Hinderstein is a board certified obstetrician-gynecologist. Tr., vo. 2, at 218. He does not have an advanced degree or sub-specialty in reproductive endocrinology or pharmacology. Tr., vo. 2, at 223. Dr. Hinderstein's testimony at trial was based solely upon published articles he read during seven hours in which he did research in preparation for his testimony. Tr., vol. 3, at 355-56.

[3]Dr. Harralson is a board certified pharmacologist who teaches at the School of Pharmacy of the University of the Pacific. He has a bachelors degree in chemistry, a Pharm.D, and a postdoctoral fellowship in Pharmacokinetics. Tr., Vol. 4, at 608-609.

Harralson's testimony, and reviewing the articles upon which they purported to base their opinions, the court finds that Plaintiffs' evidence of causation is insufficient to satisfy the Daubert standard. Plaintiffs' evidence shows, at most, that there is anecdotal support for the hypothesis that an unexplained interaction between certain antibiotics and oral contraceptives may reduce the effectiveness of the contraceptives. However, Plaintiffs' evidence falls far short of the proven, cause-and-effect relationship that is necessary to satisfy the Daubert standard.

Plaintiffs' witnesses did not cite to any competent scientific evidence to support their testimony. Although Drs. Hinderstein and Harralson claimed that their opinions were supported by numerous scientific articles[4], a careful reading of

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[4]These articles included: "Antibiotic Interference with Oral Contraceptives," 122 Journal of the American Dental Association 79 (1991); R. Bainton, "Interaction Between Antibiotic Therapy and Contraceptive Medicine," Oral Surgery, Oral Medication and Oral Pathology, May 1986, at 453-455; Michael L. Barnett, "Inhibition of Oral Contraceptive Effectiveness by concurrent Antibiotic Administration," 56 Journal of Periodontology 19 (1984);George K. B. Sandor & Kenneth F. Uffen, "Antibiotic Administration and Oral Contraceptive Failure: A drug Interaction to Note," 10 Journal of the Canadian Dental Association 775 (October 1987); Timothy G. Donley & Richard F. Smith, "Reduced Oral Contraceptive Effectiveness with Current antibiotic Use: A Protocol for Prescribing Antibiotics to Women of Childbearing Age," 11 Compendium of Continuing Education in Dentistry 392

these articles reveals that many of their authors came to different conclusions than Plaintiffs' witnesses did. In other words, Plaintiffs' witnesses took data from articles that found no statistically significant correlation between antibiotic use and increased failure of oral contraceptives, and used the data to reach a conclusion contrary to the articles' own authors. This tactic does not qualify as good science.

For example, Plaintiffs' witnesses relied heavily upon the Back article to support their testimony. this article contains the author's discussion of findings he made while studying 7 women who were taking oral contraceptives and ampicillin concurrently. At trial, Plaintiffs' experts testified that the Back study showed a drop in effectiveness of the oral

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(June 1990); Margaret J. Sparrow, "Pill Method Failures", New Zealand Medical Journal, February 1987, at 102; Gillian M. Shenfield & Judith M. Griffin, "Clinical Pharmokinetics of Contraceptive Steroids," 20 Clinical Pharmokinetics 15 (1991); D.J. Back, et al.,"The Effects of Ampicillin on Oral Contraceptive Steroids in Women," British Journal of Clinical Pharmacology, vol. 14, at 43-48 (1982); Chad I. Friedman, et al., "The Effect of ampicillin of Oral Contraceptive Effectiveness, " 55 O bstetrics & Gynecology 1,at 33 (January 1980); J.V. Joshi, "A Study of

Interaction of Low-Dose Combination Oral Contraceptives with Ampicillin and Metronidazole," 22 Journal of Contraception 643 (1980); Helena Trybuchowski, "Effect of Ampicillin on the Urinary Output of Steroidal Hormones in Pregnant and Non-Pregnant Women," Clinica Chinmica Acta, vol. 45,at9 (1973).

contraceptives in two of the seven women. Tr., vol. 1, at 75-76, vol. 4, at 646-47. However, this conclusion is in direct contradiction to the article itself which concludes with the sentence: "Ampicillin did not lower plasma oral contraceptive steroid concentrations in this study and we would suggest, based on this, that women taking oral contraceptive steroids do not need to take alternative contraceptive precautions when prescribed ampicillin." Back supra note 4, at 47.[5]

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[5]Drs. Hinderstein and Harralson also erroneously relied upon the Joshi and Friedman articles.

In the Joshi Article, the researchers set up three groups of women, all of whom were using oral contraceptives. Six of these women were given ampicillin, ten were given another antibiotic called metronidazole and a control group of an additional ten was given nothing. None of the women on ampicillin ovulated, two women on metronidazole ovulated, and one woman in the control group ovulated. According to Plaintiffs' experts, this data demonstrates that antibiotics interfere with oral contraceptives. Tr. at 650-651. However, this testimony again runs contrary to the conclusion drawn by the author of the article which was that neither ampicillin or metronidazole affected contraceptive steroid levels. Joshi, supra note 4, at 651.

In the Friedman article, the author studied 11 women on oral contraceptives who were given ampicillin. Two of the 11 women showed break-through bleeding during the study, which Plaintiffs' witnesses claimed is an indication of lack of oral contraceptive effectiveness. Tr., vol. 4, at 649-650. However, yet again this testimony conveniently ignores the concluding sentence of the atricle which states: "Most important, ampicillin appears

Furthermore, the only articles that actually tend to support Plaintiffs' experts are not based on controlled, scientific studies of the topic. Instead, they are all anecdotal case reports, reviews of research done by other people, or studies lacking a control group.

For example, in the Sparrow article, the author made a study of 163 women who became pregnant while using oral contraceptives. She found that 27 of the women had experienced previous pill failures, 81 were smokers, 29 had menstrual disturbances and 37 were on antibiotics. Notably, 59 women had none of the predisposing factors above. Sparrow, supra note 4, at 102-103. Plaintiffs' witnesses testified at trial that this study showed that antibiotics caused an increased likelihood of pill failure. Tr., vol. 2, at 238-242. This testimony is obviously not based on good science.[6] The study had no control group, and included no accounting for

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unlikely to diminish the effectiveness of the oral contraceptive studied."
Friedman, supra note 4, at 36.

[6]Using Plaintiffs' fallacious method of arriving at causation, one might cite the Sparrow study as standing for the proposition that the most likely cause of Karyn's pregnancy was her half-a-pack-a-day smoking habit. Tr., vol. 1, 80-81. After all, the women Dr. Sparrow studied were more that twice as likely to be smokers than to be taking antibiotics (81 were smokers while only 37 were on antibiotics).*

women who were on both oral contraceptives and antibiotics but who did not become pregnant.[7] At most, the study suggests that antibiotic use may be a risk factor for women using oral contraceptives. It does not, however, demonstrate a sufficient level of causation to be admissible on this issue at trial.[8]

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[7]When discussing the results of her research, Sparrow herself comments that her evidence is "anecdotal," and that "the lack of controls in this study, i.e. the number of women on various antibiotics who did not become pregnant, limits the interpretation."

[8]Drs. Harralson and Hinderstein also cited to the Swenson abstract and the Shenfield & Griffin article to support their theory of causation. However, neither of these articles even comes close to being a controlled scientific study of the subject.

In Swenson, which is only an abstract and was never actually published as a full-fledged article, the author made a study of five women on oral contraceptives and either tetracycline or ampicillin. Swenson concluded that the measured excretion of estrogen in the women's urine declined when they were taking antibiotics and oral contraceptives together as opposed to when they were taking only oral contraceptives.

In Shenfield & Griffin, the authors studied only one woman who was on oral contraceptives and minocylcine. They concluded that the woman's levels of estrogen were lower when she was on minocycline. Shenfield & Griffin, supra note 4, at 32.

The extremely small size of these studies makes them statistically insignificant. Furthermore, neither of these articles determined whether the women studied actually ovulated, and

Plaintiffs' reference to the package labelling for Triphasil-28 as proof of causation is not sufficient either. The label merely warns that certain antibiotics may "possibly" have an effect on oral contraceptive effectiveness.[9] This language is even less probative than the inconclusive studies upon which Plaintiffs' witnesses relied. Furthermore, the inclusion of a boilerplate warning on a drug package insert may reflect no more than an overly cautions response to possible liability, not scientific proof of causation.

In sum, Plaintiffs' witnesses did not rely on a single controlled study that showed a statistically significant correlation between antibiotic use an decreased effectiveness of oral contraceptives. Consequently, the Court finds that Plaintiffs' evidence does not satisfy the first prong of the Daubert standard.

B. Relevancy

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neither accounted for the independent contraceptive effect of progestin, see infra section II.B.1.

[9]The package label for Triphasil-28 states: "Certain drugs may interact with birth control pills to make them less effective in preventing pregnancy or cause an increase in breakthrough bleeding. such drugs include rifampin, drugs used for epilepsy such as barbiturates (for example, phenobarbital), and phenytoin (dilantin is one brand of this drug), phenylbutazone,(Butazolidin is one brand), and possibly certain antibiotics. YOu may need to use an additional method of contraception during any cycle in which you take drugs that can make oral contraceptives less effective."

Scientific evidence must also meet the "fit" requirement by having a valid scientific connection to the inquiry at issue in the case. Daubert, 509 U.S. at 591; Dauber, 43 F.3d at 1320. The "fit" requirement pertains primarily to the relevance of the evidence under Fed. R. Evid., but also recognizes the special dangers inherent in scientific expert testimony. Daubert, 509 U.S. at 591; Daubert, 43 F.3d at 1321 n.17. Such testimony "'can be both powerful and quite misleading because of the difficulty in evaluating it.'" Daubert, 509 U.S. at 595 (quoting Weinstein, Rule 702 of the Federal Rules of Evidence is Sound: It Should Not Be Amended, 138 F.R.D. 631, 632 (1991). Therefore, a federal judge should exclude scientific expert testimony under the second prong of the Daubert standard unless he is "convinced that it speaks clearly and directly to an issue in dispute int he case." Daubert, 43 F.3d at 1321 n.17.

Here, as mentioned previously, Plaintiffs' scientific evidence was proffered to show causation. Under California law, the plaintiff has the burden of proving causation to a reasonable medical probability based on competent medical testimony.[10] The plaintiff must show both: (1) general causation-that the defendant's conduct increased the likelihood of injury; and (2) specific causation- that the

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[10]Because Plaintiffs brought this action under the Federal Tort Claims Act, California state law substantively governs. 28 U.S.C. § 1346(b); Hines v. United States, 60 F.3d 1442, 1448 (9th Cir. 1995)

defendant's conduct was the probable, not merely a possible, cause of the injury. Jones v. Ortho Pharmaceutical Corp., 163 Cal. App. 3d 396, 402-03, 209 Cal.Rptr. 456, 460 (1985); Dauber, 43 F.3d at 1320.

1. General Causation: Interaction between Penicillin-VK and Triphasil-28

To show general causation, Plaintiffs were required to demonstrate that there is a scientifically validated interaction between Penicillin-VK and Triphasil-28 birth control pills that made it more likely that Karyn would become pregnant while taking both drugs than if she were merely taking birth control pills alone. Here, even if Plaintiffs evidence had survived the first prong of the Daubert standard, it still does not meet the fit requirement.

To the contrary, Plaintiffs' entire theory of causation is flawed. Plaintiffs' witnesses testified that antibiotics kill bacteria in the digestive system, thereby interfering with the mechanism by which oral contraceptives release estrogen into the woman's body. This lowering of estrogen levels supposedly reduces the contraceptive effect of the birth control pills and allows the woman to ovulate and become pregnant. Tr., vol.2, at 243-48, vol. 4, at 643.

However, Triphasil-28 birth control pills have two components, estrogen and progestin. Each component has independent contraceptive effect.[11] The progestin component

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[11]During their testimony, both Dr. Hinderstein and Dr. Harralson admitted that progestin has an independent contraceptive

is metabolized in a different way than the estrogen component, and Plaintiffs' experts presented no scientific evidence whatsoever demonstrating that antibiotics interfere with metabolization of progestin. [12] Therefore, even assuming that scientific evidence showed that antibiotics interfered with the estrogen component, the progestin component would still prevent pregnancy.

2. Specific Causation: Probable Cause of Karyn's Pregnancy

To show specific causation, Plaintiffs had to demonstrate that the interaction between Penicillin-VK and Triphasil-28 birth control pills was the probable, not merely a possible, cause of Karyn's pregnancy. Under Daubert, Plaintiffs could carry this burden if they could show that such an interaction occurs at more than double the rate of the known failure rate for oral contraceptives alone. 43 F.2d at 1320 ("plaintiffs must establish not just that their mothers' ingestion of Benedictin(sic) increased somewhat the likelihood of birth defects, but that it more than doubled it")

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effect. In fact there are several oral contraceptives on the market that contain only progestin. Tr., vo.3, at 359, vol.4, at 753.

[12]The only evidence that even hints at antibiotic interference with progestin levels is in the Trybuchowski article, where the author observed that one woman's progestin levels dropped while on ampicillin. Trybuchowski, supra note 4, at 9. However, this is clearly just an anecdotal observation, not the result of a broad-based, statistically valid study of the subject.*

Here, Plaintiffs have utterly failed to present any competent testimony on this issue. As mentioned previously, none of the articles cited by Dr. hinderstein or Dr. Harralson contain a controlled, broad-based study of the existence of an interaction between antibiotics and oral contraceptives, let alone the rate at which such an interaction occurs. Given that over 14 million women in the United States are currently using oral contraceptives, and an unknown number of them are prescribed antibiotics from time to time, Plaintiffs' reliance on studies involving only a handful of women is clearly not statistically defensible.[13]

II. Plaintiffs' Case

Liability for negligence under California law requires proof of the following elements: (1) a legal duty of care; (2) a breach of that duty; and (3) causation. Ann M. Pacific Shopping Ctr., 6 Cal. 4th 666, 673, 25 Cal. Rptr 2d 137, 141 (1993). In this case, even if the court had found that Plaintiffs' scientific evidence was sufficient under DAUBER to proceed to the trier of fact, Plaintiffs have still failed to meet their burden of persuasion on: (2) duty of care - whether the Army doctors were required to warn Karyn that antibiotics might interfere with the effectiveness of her birth control pills; and (2) causation - whether Karyn became

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[13]Nor did Plaintiffs establish the general background failure rate for oral contraceptives. The testimony on this issue was wholly inconclusive, ranging rom a rate of less that 1 percent to more than 8 or 9 percent.

pregnant while she was taking the antibiotics.

A. Legal Duty: Informed Consent

Under California law, a physician has a duty "of reasonable disclosure of the available choices with respect to proposed therapy and of the dangers inherently and potentially involved." Arato v. Avedon, 5 Cal. 4th 1172, 1183, 23 Cal. Rptr. 2d 131, 138 (1993) (en banc) (quoting Cobbs v. Grant, 8 Cal. Rptr. 3d 229, 242, 104 Cal. Rptr. 505, 514 (1972); Hanna v. United States, 845 F. Supp. 1390, 1392 (E.D. Cal. 1993). this duty does not required the physician to conduct a "mini course in medical science" or to discuss "the relatively minor risks inherent in common procedures, when it is common knowledge that such risks inherent in the procedure are of very low incidence." Cobbs, 8 Cal. 3d at 244-45, 104 Cal. Rptr. at 515; See also, Arato, 5 Cal. 4th at 1186, 23 Cal. Rptr. 2d. at 139-140. However, when recommending treatment, the physician must disclose any known risks of death or serious bodily injury and must explain in lay terms the complications that might possibly occur. The physician must also disclose "such additional information as a skilled practitioner of good standing would provide under similar circumstances." Arato, 5 Cal. 4th at 1190, 23 Cal. Rptr. 2d. at 143.

Most often, determining whether a potential risk is material enough to require disclosure is a question of fact that does not necessitate the admission of expert testimony. However, in certain situations, expert testimony concerning the standard of care in the medical profession may help the

trier of fact to determine whether a physician had a duty to disclose a potential risk. Arato, 5 Cal. 4th at 1191, 23 Cal. Rptr. at 143-44.

In this case, reference to expert testimony is appropriate to assist the Court, as the trier of fact, in determining whether a warning of the possible interaction between Penicillin-VK and Triphasil-28 was required. Such testimony is helpful to the court in interpreting the complex and conflicting scientific evidence as to whether, and how often, such an interaction actually occurs.

At trial, both sides presented witnesses to testify whether the Army doctors were or were not required to warn Karyn that the penicillin they prescribed for her could interfere with the effectiveness of her birth control pills.[14]

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[14]Plaintiffs called Dr. Hinderstein and a dentist, Dr. Grace, DDS Dr. Hinderstein stated that he and the other members of the obstetrics/gynecology department of Silas B. Hayes Hospital had routinely made such warnings since at least early 1992.* Tr., vol.,1, at 90. Dr. Grace stated that he had been giving such warnings in his practice since he read an article in the Journal of the American Dental Association in December 1991. Tr., vol. 1, at 157-58.

Defendant called Dr. Caples, D.D.S., head of the oral surgery unit at Silas B. Hayes Hospital, and Dr. Murphy, Karyn's obstetrician at Ft. Ord. Both stated that the policy of the Ft. Ord dental clinic was not to give such warnings in early 1992.* Tr., vol.1, at 171-72, vol. 5, at 830-835. Defendant'sexpert witnesses, Dr. Archer, Dr. Grimes, and Dr. Roy also stated their opinions that the scientific evidence of an interaction does not warrant a warning.

After considering this testimony, as well as the other evidence presented at trial, the Court finds that Plaintiffs have failed to carry their burden of establishing that a warning was required. As discussed in Section I.A, supra, the existence of such a drug interaction is unproven and the danger of it occurring appears to be extremely remote. Consequently, the standard of care in Monterey County in early 1992 did not require a warning for this small risk inherent in the extremely common practice of prescribing antibiotics.

B. Causation: Date of Conception

Plaintiffs also failed to prove by a preponderance of the evidence that Karyn became pregnant during the time that she was taking Penicillin-VK. To the contrary, for several reasons, the Court finds that it is more likely than not that Karyn conceived before she began taking antibiotics.

First, at the time that Karyn's first pregnancy test was positive on February 19 at 9:57 a.m., it was too early for the test to sense conception that supposedly occurred on February 8 or 9. The timeline is as follows. After conception, the fertilized egg spends approximately 3 to 4 days in the fallopian tube. Then it moves into the endometrial cavity and spends an additional 3 to 4 days there. Then the egg implants

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Furthermore, Karyn herself admitted that during the 12 years she had been taking birth control pills no doctor had ever warned her about the possibility of an interaction with antibiotics. Tr., vol. 1, at 82-85.*

in the uterus. Approximately one or two days following implantation, there is detectable human chorionic gonadotrophin ("HCG") in the woman's urine. For the next thirty-five days, the level of HCG doubles every 1.4 to 1.6 days. In other words, if the HCG level is one milli international unit of HCG eight days after conception, there would be 2 milli after approximately 9.5 days, 4 milli after 11 days and so on. R., vol. 8, at 30-35, 36-40.[15]

According to its labelling, the Icon II pregnancy test administered to Karyn was sensitive to 50 milli of HCG. However, defense witness Dr. Roy admitted that in controlled laboratory trials the Icon II was able to detect levels of HCG as low as 20 milli. Tr., vol. 8, at 119. Either way, if Karyn conceived on the evening of February 8, the Icon II test could not have detected her pregnancy only 10.5 days later on the morning of February 19. As footnote 14 demonstrates, it takes at least 13 to 14 days after conception to arrive at 20

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[15]The following chart summarizes the time line:

Event	Day
Ovum in Fallopian Tubes	3 to 4 days
Ovum Implants in Uterus	6 to 8 days
HCG Becomes Detectable	7 to 10 days7 to 10 days
2 milli of HCG	8.4 to 11.6 days
4 milli of HCG	9.8 to 13.2 days
8 milli of HCG	11.2 to 14.8 days
16 milli of HCG	12.6 to 16.4 days
32 milli of HCG	14 to 17 days
64 milli of HCG	15.4 to 18.6 days

milli of HCG. If a pregnancy test administered on February 19 was positive, Karyn must have conceived, at the latest, on February 6 or 7. Conception on February 8 or 9 would not be detectable until February 21 or 22.

Second, it is highly improbable that Karyn would have been able to ovulate on February 8 or 9 if she had already taken six birth control pills on February 2 through 7. According to Dr. Archer's unrebutted testimony, the estrogen component of the Triphasil-28 pills would have inhibited Karyn's production of follicle stimulating hormone ("FSH") and luteinizing hormone ("LH") to such an extent during the first six days of her cycle that it would have prevented her follicles from enlarging sufficiently thereafter to produce an ovum on February 8 or 9. Tr., vol. 5, at 899-900. In other words, even assuming that the antibiotics interfered with the effectiveness of Karyn's birth control pills, there was not enough time after Karyn started taking the antibiotics to result in pregnancy within two days.[16]

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[16]At trial, the parties also spent much time and effort debating the significance of three ultrasounds taken of Karyn's fetus on April 30, June 10, and October 6. See Tr., vol. 2, at 293-334. In each of these ultrasounds, measurements were made of various parts of the fetus's (sic) body to determine its approximate age, and therefore the date of conception.

After examining these ultrasounds in detail, the Court finds them to be inconclusive in determining the date of Abbigayle's conception for several reasons: (1) the estimated date of conception had a margin of error of plus or minus 7 days; (2) it was unclear

CONCLUSION

Based on the foregoing, the Court finds for Defendant and against Plaintiff. Judgment will be entered accordingly.

IT IS SO ORDERED.

DATE: 7/3/96

SPENCER WILLIAMS

United States District Judge

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which of the ultrasound measurements was the most accurate; and (3) the parties' experts applied wholly incompatible methodologies as to whether the estimated date resulting from the ultrasound measurements was the conception date or merely the date of Karyn's last menstrual period.

FOR PUBLICATION
UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

Karyn Jones; Chris Jones,
Husband and Wife,
Plaintiffs-Appellants, No. 96-16643

V.

D.C. No.

CV-93-20137-SW
United States of America, **OPINION**
Defendant-Appellee.

Appeal from the United States District Court
for the Northern District of California
Spencer M. Williams, Senior District Judge, Presiding
Argued and Submitted October 6, 1997–San Francisco, California

Filed October 28, 1997
Before: Mary M. Schroeder, Robert R. Beezer and Melvin Brunietti, Circuit Judges

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COUNSEL

Donald J. Loftus, Pebble Beach, California, for the plaintiffs-appellants.

Patricia J. Kenney, Assistant United States Attorney, San

Francisco, California, for the defendant-appellee

OPINION

BEEZER, Circuit Judge:

Karyn and Chris Jones appeal from the district court's findings of fact and conclusions of law rendered in connection with their claim brought pursuant to the Federal Tort Claims Act. Defendants have moved to correct the record, and plaintiffs have moved for sanctions. We have jurisdiction and affirm.

I

In early 1992, plaintiffs[1] were married and living together at Fort Ord, California, where Chris Jones, a sergeant in the United States Army, was stationed. On January 16, 1992, plaintiff went to an Army gynecologist for an annual examination and to obtain a prescription for birth control pills. Plaintiff was not pregnant at the time of this visit. The gynecologist prescribed Triphasil-28 birth control pills, which contain both estrogen and progestin. The gynecologist did not warn plaintiff that antibiotics could reduce the efficacy of her birth control pills.

Plaintiff began taking her Triphasil-28 pills on February 2, 1992. During this time, plaintiffs had sexual intercourse nightly.

On February 7, 1992, plaintiff went to a dental clinic at Fort

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[1]"Plaintiffs" refers to the plaintiffs collectively. "Plaintiff" refers to Karyn Jones.

Ord. An oral surgeon examined plaintiff and decided she needed surgery. To assure that no infection would be present at the time of the surgery, the oral surgeon prescribed Penicillin-VK, an antibiotic. Although plaintiff's medical chart indicated that she was taking birth control pills, neither the oral surgeon nor his dental hygienist warned plaintiff that the penicillin might interfere with the effectiveness of her birth control pills.

The oral surgeon directed plaintiff to take 500-milligram pills of penicillin four times a day for six days. Plaintiff took four antibiotic pills on February 8 and 9, three pills on February 10 and 11, two pills on February 12, and one pill on February 13.

On February 19, plaintiff returned to the dental clinic to have lab work done in preparation for surgery, including a routine pregnancy test. During this visit, a different oral surgeon warned plaintiff that antibiotics could reduce the effectiveness of birth control pills.

On February 20, plaintiff was informed that her pregnancy test was positive. A second test performed on February 21 was also positive. On October 17, 1992, plaintiff gave birth to a baby girl.

II

Plaintiffs filed an administrative claim against the Army for malpractice and wrongful life. The claim was denied, and plaintiffs filed a complaint in federal court. The sole issue at trial was whether defendant was liable for costs attributable to plaintiff's pregnancy and raising plaintiffs' daughter. At trial, plaintiffs presented two expert witnesses who testified that the antibiotics prescribed to plaintiff reduced the efficacy of her birth control pills. The defendant

presented expert testimony to counter this evidence. After a two-week bench trial, the district court granted defendant's motion in limine to exclude plaintiffs' expert testimony on the ground it did not satisfy the standard set forth in *Daubert v. Merrell Dow Pharmaceuticals*, 509 U.S. 579 (1993) and *Daubert v. Merrell Dow Pharmaceuticals, 43 F.3d 1311 (9th Cir. 1995)*. The district court also concluded that plaintiffs failed to establish other elements of their case, including duty to warn and causation. This appeal followed.

On appeal, plaintiff contend that, among other things, the district court erred in finding plaintiffs failed to prove by a preponderance of the evidence that plaintiff became pregnant during the time she was taking penicillin. We review for clear error the district court's factual findings in connection with a bench trial. **Saltarelli v. Bob Baker Group Med. Trust, 35 G.4f 483, 384 (9th Cir. 1994)**. We must accept the district court's findings of fact unless we are left with the definite and firm conviction that a mistake has been committed. **Committee for Idaho's High Desert, Inc. v. Yost,** 92 F.3d 814, 819 (9th Cir. 1996) (quoting United States v. United States Gypsum Co., 333 U.S. 364, 395 (1948)). If the district court's "account of the evidence is plausible in light of the record viewed in its entirety," we may not reverse even if we are convinced that had we been sitting as the trier of fact, we would have weighed the evidence differently. Phoenix Eng'g and Supply Inc. v. Universal Elec. Co., 104 F.3d 1137, 1141 (9th Cir. 1997) (quoting Anderson v. Bessemer City, 470 U.S. 564, 573-74){1985)

III

[1] Plaintiff tested positive for pregnancy on the morning of February 19, 1992; the pregnancy test used was the Icon II test. The Icon II test detects human chorionic gonadotrophic ("HCG"), which is produced in increasing amounts approximately seven to ten days after conception. The district court found that it takes at least 13 to 14 days after conception for levels of HCG to be detectable by the Icon II pregnancy test. In light of the Icon II test's sensitivity to HCG, plaintiff must have conceived 13 to 14 days prior to February 19. Accordingly, plaintiff must have conceived prior to the time she began taking penicillin on February 8. Review of the record indicates this finding is not clearly erroneous.

[2] Plaintiffs contend that the Icon II test detect HCG within ten days of conception, and that the positive test on February 19 is therefore not inconsistent with a date of conception of February 9. Plaintiffs refer to the Icon II test package insert, which indicates that the test is "sufficiently sensitive to show positive results as early as one week after implantation, or 4-5 days before the first missed menses." Plaintiffs take this to mean that the test can detect a pregnancy in nine to ten days. Sensitivity to one week after implantation is not inconsistent with the district court's findings because implantation takes place six to eight days after fertilization. *See Jones v. United States,* 933 F. Supp. 894, 902 n.15 (N.D. Cal. 1996)

IV

[3] Plaintiffs contend that ultrasound evidence and calculations based upon plaintiff's first day of bleeding of her last

menstrual period, or "LMP", indicate that plaintiff conceived on February 9. For example, plaintiffs claim plaintiff's LMP was on January 27, 1992, indicating that her next menses should have begun on February 23 or 24. Ovulation and conception on the fourteenth day of her cycle would indicate that the date of conception was February 9. The district court, however, specifically rejected the ultrasound evidence as inconclusive, a finding which, in light of the record, cannot be said to be clearly erroneous.

[4] In addition, the district court found that it was highly improbable that plaintiff would have been able to ovulate on February 8 or 9 if she had already taken six birth control pills on February 2 through 7. *Id.* at 903. The district court explained that the estrogen component of the Triphasil-28 pills inhibits production of two hormones, follicle simulating hormone and luteinizing hormone, which are necessary for production of the ovum. The Triphasil-28 pills plaintiff took on February 2 through 7 would have inhibited these hormones to such an extent that plaintiff could not have produced an ovum on February 8 or 9. Thus, the district court found, even if the penicillin eliminated the effect of the estrogen, there was not enough time for plaintiff to become pregnant within two days. This finding is not clearly erroneous.

V

We conclude that the district court's finding that plaintiffs failed to establish that plaintiff became pregnant while taking penicillin was not clearly erroneous. We need not address plaintiffs'

other arguments.[2]

AFFIRMED.

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[2]Plaintiffs contend there were denied their right to a fair trial because the district court judge was biased against them. The record does not support this claim.

Defendant moved pursuant to Rule 10(e) of the Federal Rules of Appellate Procedure to correct the record. Defendant previously moved the district court, and the district court denied the motion because the errors were insignigicant spelling and typographical errors. We agree, and deny the motion.

Plaintiffs' motion for sanctions is also denied.

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

Karyn Jones; Chris Jones, Husband and Wife,
Plaintiffs-Appellants,
v.
United States of America,
Defendant-Appellee.

No. 96-16643

D.C. No. CV-93-20137SW

ORDER

Filed: Jan 9, 1998

Before: Schroeder, Beezer and Brunetti, Circuit Judges.

The Panel has voted unanimously to deny the petition for rehearing. Judges Schroeder and Brunetti vote to reject the suggestion for rehearing en banc and Judge Beezer so recommends.

The full court has been advised of the suggestion for rehearing en banc and no judge in active service has requested a vote to rehear the matter en banc.

Pursuant to Rule 35 (b) of the Federal Rules of Appellate Procedure, the petition for rehearing is denied and the suggestion for rehearing en banc is rejected.

Testimony of Dr. Hinderstein:

12696,335: 12 Well, the letter states, "Dear Dr. Hinderstein."
13 In the second paragraph, "Among heath care
14 professionals, there appears to be a consensus of opinion that
15 an interaction between certain antibiotics and oral
16 contraceptives is possible. It has been suggested that the
17 antibiotics which alter the gastrointestinal flora (such as
18 penicillin or tetracycline) may reduce oral contraceptive
19 efficacy ... Alteration of the GI flora by antibiotics could
20 interfere with this process."
21 THE COURT: Where did you skip to?
22 BY MR. LOFTUS
23 Q Why don't you read the whole thing?
24 A "This concept is based on the metabolism of ethynyl
25 estradiol (EE), which undergoes extensive first-pass metabolism,

0336
01 during which it is conjugated in the liver. The GI flora
02 produce enzymes which hydrolyze these conjugates of EE, thereby
03 allowing free EE to be reabsorbed in a process known as
04 entero-hepatic recirculation. Alteration of the GI flora by
05 antibiotics could interfere with this process, thereby
06 decreasing plasma EE levels. Therefore, contraceptive failure
07 is possible." (12696)

Testimony of Dr. Hinderstein:

0242

MR. LOFTUS: If it would please the Court, could Dr. Hinderstein step to the chart and perhaps use some drawings to explain this process to the Court?

THE COURT: Yes, indeed.

THE WITNESS: The important concept that I believe is in play here, and if I may use EE as a code word for ethynyl estrodiol, which is the active molecule in the birth control pill that we believe may confer or have most important role in protecting the woman from getting pregnant. So I'm going to use EE so I don't have to say ethynyl estradiol many more times than its said.

0243

If I could diagrammatically show that the pill is swallowed and entered beyond the stomach into the small bowel, in the small bowel, approximately 40 percent of it gets absorbed in the active form. And in order for it to work, it must be active, not covered with anything.

Okay. 60 percent gets what we call bound by other molecules in the gut wall and in the liver. So 60 percent of the active product is now inactivated by the small bowel cells which will suffocate it, and when you get into the liver, it'll be hydroxilated and glucuronide is added to it. And what all this means is on this active molecule are put balls to protect it so it no longer becomes active so the body can get rid of it

so it won't be in the body all day for the rest of your life.

THE COURT: How does that work?

THE WITNESS: 40 percent is actually passed and 60 percent now gets bound of the dose of the pill. So 60 --

THE COURT: Which is around to help prevent pregnancy?

THE WITNESS: The 40 percent is still operative and the 60 percent is bound. It goes to the liver. The liver binds it even more to protect it so it doesn't get destroyed, and then from the liver it gets passed in the bile to the large bowel.

Here in the large bowel, there are bacteria that break off all of these balls that the liver has nicely put on to protect it, liberating once again the active hormone so it can

0244

do its work so that you get a 24 hour coverage period. If you just put on the 40 percent, within a couple hours that effect is gone and the woman is protected for only a couple of hours.

By having it circulated, I guess the best way I could put it, it's like a time release capsule that you take of medication. This second pass now confers upon the lady another protective time frame until she can take the pill the next day.

THE COURT: It's again in the reproductive system then at that time?

THE WITNESS: The only way it can get in the reproductive system is when it's active to do its work. So the first time when it gets out of the small bowel at 40 percent, it comes back in and then gets broken down, so it becomes active again for the second time and that can be anywhere from four to

six hours. Several studies have shown there are peaks of this at different times throughout the day at 4:00 and 6:00 o'clock which they believe is this recirculation.

THE COURT: So the 40 percent that doesn't go to the bowel is still functional to help birth control while it goes through the system?

THE WITNESS: It goes through the blood system and eventually gets to the liver where the liver now binds it again. The body has to get rid of a medication one way or the other, either through the liver or kidneys or the lungs. Something has to get it out or else that pill will be in there for the rest of

0245

your life.

So there are -- the 40 percent that becomes active and goes to the uterus and goes to the ovaries will now recircle back to the blood vessels into the liver, the liver will bind it, and that may be the one at eight hours that's given us.

BY MR. LOFTUS

Q So it comes back into the large bowel and the balls are taken off again?

A Right, exactly. When it comes back through the liver, the only way the liver can get rid of it is through the bile into the bowel.

THE COURT: Bile or bowel?

THE WITNESS: Bile to the bowel.

THE COURT: Then it is eliminated from the system?

THE WITNESS: Eventually it is, because the bacteria can't digest all of these metabolites all the time, so eventually it has made enough passes and it gets by.

Percentage

wise, an amount will finally be eliminated. That's why you have to take a pill every day.

THE COURT: So you have this going all the time?

THE WITNESS: Correct.

THE COURT: But if I took one pill, how long before it's eliminated from my system?

THE WITNESS: 24 hours. That's why you have to take a pill the next day.

0246

THE COURT: So that double circulation all occurs within 24 hours?

THE WITNESS: Yes. Now, if we throw into this some penicillin, what we do is we kill the bacteria in the gut that is responsible for breaking down --

THE COURT: Is that a medical term, gut?

THE WITNESS: Yeah. I always use "gut".

THE COURT: Okay.

THE WITNESS: So we throw the antibiotic in, the antibiotic destroys those bacteria, those bacteria did not break off all those balls that are on the inactive hormone, and the poor lady is now left without her protection for the rest of the day. And that is the --

THE COURT: It certainly weakens the bacteria. They can't do the job?

THE WITNESS: Penicillin is a bacteriocidal drug, and "cidal" means killer. There are certain antibiotics which will slow the growth or stop the reproduction. There's all

different classes of antibiotics that do different things.

THE COURT: There's good buys and bad guys?

THE WITNESS: That's true. That's the problem of antibiotics, they can kill good guys, like the clostridium in the bowel. A cidal drug, it kills the bacteria, it doesn't just slow them down, and it kills them fast.

There's my physiology for today.

0267

THE COURT: It confuses me. How can you show that a particular antibiotic is effecting a specific function? They may effect different organs and have the same adverse result; correct?

0268

THE WITNESS: Not antibiotics. We're talking, at this point, about the estrogen. The antibiotics, that's a whole different gang because it's effecting the bacteria, not the body.

THE COURT: The effect on estrogen may be from several causes?

THE WITNESS: The effect to prevent pregnancy, we know of three possible ways. The mucous that comes out of the cervix becomes hostile so the sperm can't penetrate, so there's a form of birth control. The lining of the uterus becomes inactive so the egg, even though it's fertilized, may not be able to implant. The bed is not made and it's not ready to sleep in. Or it could suppress the ovulation, and without ovulation, you can't get pregnant.

THE COURT: So penicillin or something else

wouldn't
17 effect those functions?
18 THE WITNESS: No. But penicillin is effecting the
19 hormone, the estrogen, that is needed to protect it.
20 THE COURT: By the penicillin killing the bacteria?
21 THE WITNESS: By killing the bacteria which break
22 off that covering on the active molecule so it can't be
23 reabsorbed back and to protect her.
24 BY MR. LOFTUS
25 Q That in turn may have an effect, even though it's
0269
01 not shown to be significant on the estrogen level, it may be
02 sufficient to effect one of these three contraceptive
03 mechanisms?
04 A That's correct. The point is if you just focus on a
05 level in the blood, you're not focussing on what organ needs
06 that level, and maybe that organ needs a higher level and that
07 group of patients just right on that line where the slightest
08 interaction, be it penicillin or whatever, can drop them below
09 that safe level.
10 THE COURT: So penicillin effects the bacteria and
11 that may effect other things which would cause the removal, the
12 inhibiting effects, of a birth control pill?
13 THE WITNESS: Correct. Exactly right.
0247
01 BY MR. LOFTUS
02 Q Now Doctor, do you have an opinion, based on
03 reasonable medical probability, as to the mechanism by which
04 penicillin interferes with the efficacy of oral contraceptives?
05 A That was exactly it. The penicillin will destroy a

06 sufficient number, or all, of the clostridia or the type of
07 bacteria that will take the inactive, take the inactive hormone
08 and convert it to an active form that will be, we believe, the
09 protective mechanism for conception.
10 Q So the demonstration and the explanation that you
11 just gave to the Court is, in your opinion and based on your
12 reasonable medical probability, the mechanism by which
13 penicillin interferes with the efficacy of oral contraceptives?
14 A And based on the literature which supports this
15 theory and has been brought up in several articles as to the
16 cause.

257

14 Q Doctor, if you are interested in determining, or
15 attempting to determine, whether a particular scientific theory
16 has gained general acceptance within your field of expertise,
17 where do you go to make that determination?
18 A There's several publications that bring out both
19 surveys, which are abstracts of other articles, and there are --
20 the American College Monthly sends out warnings and also
gives
21 us drug evaluations; the American Medical Association in their
22 Drug Evaluations; the P.D.R.; and I do get innumerable
numbers
23 of mailers from both the F.D.A., drug companies and other
24 organizations that are out to advise us of any complications or
25 problems that we should be aware of.

0258

01 Q So in summary, article 144 is a source referred to
02 you to determine whether a particular scientific theory has

gained general acceptance?
A That's correct.
Q And please tell us what significance the A.M.A.'s Sixth Edition Drug Evaluation, Plaintiff's Exhibit 144, is in your evaluation?
A On page 190, on the second column, second paragraph, under the main title of Interactions that Decrease the Efficacy of Oral Contraceptives, and I quote --
THE COURT: 190? Page 190?
THE WITNESS: Page 190. It's the second paragraph down of the second -- I think you have it right there to your right.
THE COURT: 1190?
THE WITNESS: 190.
MR. LOFTUS: 1190.
THE WITNESS: I have 190 on mine.
MR. LOFTUS: It should be 1190.
THE WITNESS: Do we have the same -- yes, this paragraph right here.
THE COURT: It's page 1190.
THE WITNESS: Mine was cut off.
THE COURT: Okay.
THE WITNESS: Sorry.

0259

THE COURT: Okay. Page 1190, third paragraph in the second column.
THE WITNESS: Second column, second paragraph.
THE COURT: "On two occasions"?

THE WITNESS: "A few case reports of possible interaction with antibiotics, including ampicillin and tetracycline, appear to indicate that contraceptive effectiveness, (eg, breakthrough bleeding, pregnancy) may decrease with concomitant use."

The second line from that says the "destruction of bacterial flora in the gut. Normally, bacterial enzymes hydrolyze hormone conjugates, freeing the steroid for reabsorption by the gut."

BY MR. LOFTUS

Q The second sentence where it says, "The suggested mechanism is" --

A Enterohepatic recirculation.

Q -- "due to the destruction of bacteria flora in the gut," is that essentially what you explained to His Honor with the chart?

A Yes.

Q And this is the A.M.A.'s representation in 1995?

A That's correct.

ABSTRACTS OF PAPERS, GASTROENTEROLOGY Vol. 78, No. 5, Part 2 Page 1332:

Effect of antibiotics on fecal/urinary excretion of ethinyl estrodiol, an oral contraceptive. L. Swenson, B. Goldin, S.L. Gorbach, Tufts-New England Medical Center, Boston, MA.

Estorgens, like bile salts, have been shown to undergo extensive enterohepatic circulation. Approximately 60% of circulating estrogen are excreted in the bile, conjugated as glucuronides and/or sulfates. They are deconjugated by intestinal bacteria, whereupon the estrogen are reabsorbed. Oral ampicillin reduces urinary excretion of endogenous estrogen with an increase in fecal excretion, presumably by suppressing bacterial deconjugation. Occasionally, women receiving oral contraceptives and antibiotics simultaneously have experienced breakthrough bleeding and become pregnant. We studied 5 women, ages 24-31, who wer given thinly estrodiol (EE@), cycled 30 ug/day for 21 days, then 7 days off, for 3 mos. Mechanical contraceptives were also used. During the 2nd and 34d mos, they were given asingle pulse dose of 25 uCi 3H-EE2 on day 15; urine and feces were collected for 96 hrs and the radiolabeled drug was counted. Bacterial estrodiol-B-glucuronidase (E2-BG) was measured in fresh feces. During the 3rd mo, a 10-day course of oral tetracycline, 250 mg qid (4 women) or ampicillin , 250 mg qid (1 woman) was started on day 13. The excretory pattern of labeled EE2 was compared before and during antibiotics. During antibiotics 3/5 women (2 tetracycline, 1 ampicillin) had decreased urinary excretion (before-51% of recovered

dose excreted in urine vs 35% on antibiotics) and increased fecal excretion (before-48% excreted in feces vs 64% on antibiotics); the level of fecal bacterial enzyme E2-BG also fell during antibiotics. 4 of 5 women had rapid urinary excretion of EE2 on antibiotics, with a mean half-time before antibiotics of 27.8 hours, compared to 18.7 hours on antibiotics. One woman showed no change on antibiotics in fecal/urine excretion and E2-BG, and a slight increase in half-time of urinary excretion. **These studies suggest that metabolism of exogenous estrogen contraceptives is influenced by tetracycline and ampicillin, probably by inhibiting bacteria that deconjugate estrogen**. In some women (3/5 in our small series), these antibiotics produced rapid elimination of EE2 and a shift toward increased fecal and decreased urinary excretion.(Emphasis supplied)

Clinical Pharmacokinetics of Contraceptive Steroids An Update, Shenfield and Griffin, Clin. Pharmacokinet. 20(I); 15-37, 1991:

Beginning at page 31:

"Other antibiotics

This is as controversial topic and, although there have been further studies since 1983, the issue is far from resolved. There have been numerous anecdotal, but well documented, reports of pregnancies and breakthrough bleeding occurring when women on oral contraceptive steroids take a course of broad spectrum antibiotics. It has been suggested that the mechanism is antibiotic suppression of intestinal commensal

bacteria resultling in decreased enterohepatic recirculation of ethinylestradiol and hence reduced plasma hormone concentrations (Shenfield 1986). ...

It is clear that significant interactions do not occur in all (or possibly even in most) women, perhaps due to the development of resistant bacteria with prolonged antibiotic therapy (Orme & Back 1986). The situation is further complicated by the fact that gut microflora vary in response to changes in diet, fluid intake and geography. For example, 'omnivorous' women have higher circulating levels of estrone and estradiol and higher urinary estriol3-glucuronide excretion than do vegetarians, which suggests that reduced enterohepatic reabsorption of estrogen occurs in the latter (Goldin et al. 1982). Against this 'background noise' there are consistent suggestions that some women do have breakthrough bleeding or pregnancies as a result of interactions with antibiotics (Kovacs et al. 1989; Sparrow 1987, 1989). Back et al. (1988) reviewed reports from 1968 to 1984 to the UK Committee on Safety of Medicines concerning interactions between oral contraceptive steroids and antibiotics. It is well recognized that such reports are only the tip of the iceberg. 63 pregnancies were reported, involving a wide range of antibiotics of which 70% were penicillin and tetracylines. Five cases of a cotrimoxazole-associated pregnancy were reported. The authors reached the very reasonable conclusion that 'individuals at risk are most probably (but not exclusively) women with a low bioavailability of ethinylestradiol due to extensive steroid

metabolism in the gut wall and liver; a large enterohepatic circulation of ethinylestradiol and a particularly susceptible gut microflora able to hydrolyse steroid conjugates". The present author's own studies would support this view; women on any doese of oral contraceptive steroids, with very low trough plasma concentrations of thinylestradiol, with or without low levonorgestrel concentrations, have been found to be more likely to have breakthrough bleeding (Shenfield et al. 1989) Since trough oral contraceptive steroid concentrations have been show to correlate well with 24-hour AUC (Kanarkowski et al. 1988), THIS SEEMS REASONABLE EVIDENCE THAT WOMEN WITH LOW ORAL CONTRACEPTIVE STEROID BIOAVAILABILITY (FOR WHATEVER REASON) ARE AT RISK OF 'PILL FAILURE'.

Figure 2 shows two 24-hour concentration versus time profiles taken at day 15 in the same woman who was on a low dose triphasic ethinylestradiol/levonorgestrel preparation. The curve showing plasma concentrations of ethinylestradiol taken without other drugs displays definite second and third peaks at 4 and 6 hours; these probably represent enterohepatic rercirculation, although they occur earlier than usually suggested for such "recirculation peaks" (Orme et al. 1983). The lower curve was taken during a cycle when the same oral contraceptive preparation was being taken together with a course of minocycline 100mg twice daily. The tmax and Cmax are the same, indicating no change in absorption of 'first-pass' metabolism via gut or liver.

However, neither of the later peaks is seen and the AUC is very much reduced (1011.1 compared with 3545.5 ng/L-h). The 24-hour concentration is also reduced, although the starting trough values had been similar. This individual had repeated breakthrough bleeding when taking courses of antibiotics and it appears that his was probably due to lower concentrations of ethinylestradiol when on the combination of drugs. No comparable changes were seen with levonorgestrel.

It is suggested that women with this type of 'sensitivity' to antibiotics are those at risk of problems. If they also have low trough plasma contraceptive steroid concentrations this risk might be increased, which could explain the observation that women on triphasic preparations are at greater risk of pregnancy (Kovacs et al. 1989). At present these women cannot be identified on clinical grounds, and therefore caution is necessary for all women taking antibiotics (except possibly cotrimoxazole) with contraceptive steroids. It is possible that regular monitoring of trough concentrations might identify an 'at risk' group of women (Shenfield 1989).

"HEALTH SCARE" REFERENCES:

Direct examination of Karyn by Mr. Loftus wherein she had just read extensively from the Birth Control package insert:

THE COURT: Did you read all this before?

THE WITNESS: Sir, I would read through it as best I could.

THE COURT: **Scared the hell out of me**, the part about the heart. **Scare the dickens out of you, won't it**? (Tr. Vol1,12495:44:9-13) (Emphasis supplied)

During defense counsel's direct examination of Defense expert, Dr. David Archer, the Judge injected his own feelings during a dialogue he initiated with Dr. Archer, twit:

THE COURT: Several articles, not on this particular subject directly, but several articles lately called information about the health care industry about some studies when they get the big stories and people think they've got a crease in their ear being subject to heart attacks. Publicity and this reports even in the New England Journal of Medicine publishes reports like this that have no scientific basis. They are interesting and anecdotal and get the good headlines. They **scare the hell out of people, but there's no good basis to do so.** It's a popular thing going on these days.

THE WITNESS: Absolutely. And I agree with that, sir.

THE COURT: They make a lot of money at that. **Anyhow, this is what we have to do.**

(TR vol121195, 982:23-984:11) (Emphasis supplied)

Later when Plaintiffs' counsel, was offering into evidence a U.S.A. report on a just published scientific study in the New England Journal of Medicine:
Cross-examination of Dr. Gimes by Mr. Loftus:

MR. LOFTUS: This is a U.S.A. Today which contains a quote from a New England Journal of Medicine report. It's date appears as December 7, 1995. The title of the article appears. It qualifies, under we respectfully submit under Section 901 of the Evidence Code, as a newspaper periodical which is self authenticating. It's a duplicate within the definition of 1004, and it's, this is Plaintiff's Exhibit 159. (Tr. Vol.121395, 1256:16-18)

THE COURT: Well, also the summary of what the newspaper puts into of an article in the New England Journal of Medicine is part of the **health scare industry**. They want something to be read or published, and it may not be what it actually said, so I would be kind of skeptical as to what they put in that paper. Is it an accurate reflection of the total report?

MR. LOFTUS: Well, it's -- I understand what the Court is saying, and I, you know, the only thing I can say is this is a well published newspaper. I would think they would value their reputation for accuracy.

THE COURT: Well, they're known to try to increase the circulation. (Tr. 121396, 1256:16-1257:13) (Emphasis supplied.)

Judge's Extra Courtroom Evidence:

By Mr. Loftus:

Q Doctor, if a male patient would present himself to you, would have presented himself to you in February of 1992, and you had determined that he needed root canal surgery and you were anticipating prescribing penicillin to him, would there be any reason for you to caution him concerning the interaction between penicillin and oral contraceptives?

A No.

THE COURT: Doctor, that's because I mentioned here that I had a root canal done and they didn't tell me about the penicillin danger. Of course, I wouldn't call it malpractice or anything else. (Tr. Vol 12495, 167:1-14)

12695,212:

MR. LOFTUS: Thank you.

The only other thing she was going to testify as to was the fact that the Army now has a written caution to any patients who they're prescribing penicillin to.

THE COURT: That's after the fact. We don't need that. The other day when I got my penicillin, right on there it says, "Penicillin for tooth treatment. If you're pregnant, if you're on birth control pills, if may have an effect." So now the drugists give it too, so it's common practice now. (Tr. Vol 12698, 212:6-14)

Judge's takes Daubert Rulings "under submission":

In response to Plaintiffs Daubert objection to Defendant's Dr. Jones' scientific testimony:

THE COURT: I'll allow the testimony. Whether I accept it as scientific testimony or summary of something else, I'll consider that and I'll give it the weight I think it deserves.

I think it's important testimony as to the history of what's going on and what the results have been, and I think the witness is well qualified to testify on that subject matter. Whether it qualifies as, quote, "scientific testimony" under Daubert is a matter I will take under submission.

MR. LOFTUS: Thank you Your Honor. Do I understand you'll make that determination later?

THE COURT: I want to hear her testimony and let her get on the airplane. I'm going to say -- well, I'll decide tomorrow and we'll put you back on the witness stand. But I'll hear the testimony, and what weight I give to it depends on how I evaluate the testimony.

I think one of your witnesses, the first one, he testified -- I let him testify. I said I will weigh and evaluate the evidence after I hear the case. He relied on the law school class opinion which I thought was a weak legal issue.

Anyhow, I'll let her testify. (Tr. Vol 12795, 563:-564:11)

Defendant's Daubert Objection to Plaintiff's Dr. Hindersteins opinion testimony:

MR. LOFTUS: The Daubert decision makes it extremely clear that you do not need to bring in an expert that has had hands-on experience or done the research that is being relied upon as a basis for the expert's testimony.

As long as the expert is qualified in the field and is able to analyze the studies that have been done by others in the field, and qualified as an expert to do that, then the law, under Daubert, is if that science that he is relying on meets the good science prerequisites of Daubert, then the, then he's qualified and he should be admitted.

THE COURT: Well, we'll have to hear the testimony, what testing has been done and how it's been done --

MR. LOFTUS: Certainly.

THE COURT: -- and falsifiability of the pieces, of the hypothesis in this particular situation. My inclination is to let him testify, and I'll see how he does on cross examination, then I'll evaluate the weight I'll give to his testimony.

MR. LOFTUS: The question was whether or not you were going to permit him, allow him, to testify as an expert.

THE COURT: I'll allow him to testify and I will evaluate whether or not it qualifies as expert testimony after I hear it. The weight I give it will be dependent upon what the testing he's talking about is in this case, and I will test it to determine whether it was or wasn't. There's a percentage that says, the percentage failed normally anyhow, how can

they say the particular failure was due to the chemical or normal failure?

MR. LOFTUS: Certainly.

THE COURT: So I will hear the testimony.

MR. LOFTUS: Thank you. (Tr. Vol. 12895, 632:13-633:23)

Court allows defendant's expert, Dr. David Archer's testimony without requiring proof of reliability:

BY MS. KENNEY

Q Back to the example I gave you of the woman who takes the Triphasil pills and then takes a pill without any ethynyl estradiol on day 7, thereafter, how many days, in your estimation, Doctor, does it take for follicular development to reach the point where ovulation could take place?

MR. LOFTUS: This is what I'm objecting to. There's no reference to that in his report, and I'd like to voir dire him on the basis.

MS. KENNEY: Your Honor, he's going to be here for cross examination.

THE COURT: Is that in the report?

MS. KENNEY: The conclusion is, yes.

MR. LOFTUS: I have the report right here. I'd like to see where the conclusion is.

MS. KENNEY: The conclusion is antibiotics do not interact with oral contraceptives to decrease their effectiveness. Part of his conclusion is based on his physiological understanding of the hormonal changes, the

follicular development in which the changes in the endometrium form during a phase of a woman not on oral contraceptives and during a phase where a woman is taking oral contraceptives, and that's what the doctor is testifying about right now.

MR. LOFTUS: Under Daubert, I believe, with all due respect, Your Honor, that we're entitled to a 104(a) hearing to see if the scientific basis for this opinion meets the Daubert requirements.

MS. KENNEY: Your Honor, Plaintiffs --

THE COURT: The testimony seems to be satisfactory as far as I'm concerned. You say it's not in the report?

MR. LOFTUS: And we don't -- and even if it was in he report, we don't know what he's a going to opine.

THE COURT: We'll accept him, as in your witnesses, until we hear the whole thing.

MR. LOFTUS: I just wanted to make a record. May I have a continuing objection?

THE COURT: You may. (Tr. Vol 121195, 897:14-898:24)

Defense counsel's examination of Defense expert Dr. Grimes:

Q Doctor, do you have an opinion, based on a reasonable medical certainty, as to whether Karyn Jones was already pregnant when she began taking penicillin on February 8, 1992?

A Yes, I do have an opinion.

Q And what is that opinion?

A That she'd already conceived before she took the first penicillin tablet.

Q With what agree of confidence do you hold that opinion?

A In excess of 95 percent medical certainty.

MR. LOFTUS: Well, Your Honor, I need to object to that and ask that be stricken until we hear the basis of his opinion.

THE COURT: They're entitled to give their opinion and then the basis and then you object. It's perfectly appropriate to give the opinion and then the basis.

MR. LOFTUS: But I just want to lodge my objections, lack of Daubert qualification and ask for 104(a).

THE COURT: Do you want to voir dire now? The bjection is noted. Do you want to voir dire now on his expertise?

MR. LOFTUS: No. She can go ahead. I just wanted to lodge my objection.

MS. KENNEY: I apologize. I would like to offer this expert in epidemiology and in obstetrics and gynecology to the Court as such, and if Counsel would like to voir dire, he certainly can.

MR. LOFTUS: Not on that. Not on that issue, but I do want to voir dire him on the opinions that he's --

THE COURT: You'll certainly have an opportunity to.

MR. LOFTUS: Thank you.

THE COURT: You can voir dire him on his general

qualifications now or you can wait for his opinions and cross examine him on that and also on his qualifications.

MR. LOFTUS: I'll wait on that.

THE COURT: Okay. You'll have your chance.

MR. LOFTUS: Thank you. (Tr. Vol 121395, 1109:08-1110:20)

Exchange following scientific expert opinion testimony elicited by Plaintiffs' counsel during cross-examination of Dr. Grimes:

By: Dr. Grimes...The final point is even if there was a complete nullification of the estrogen by this fictitious mechanism, she would still have the contraceptive effectiveness of the progestin, which she did take, and which would not be effected by the antibiotic.

So for those three reasons, this hypothesis is not tenable.

BY MR. LOFTUS

Q Well, let me see every single item of scientific literature that you rely upon as a basis for the opinion that you just gave that her missing two days of contraceptive protection by reason of her taking her four tablets of penicillin on the 8th and then taking another four on the 9th, that that would not be sufficient to allow her to become pregnant on the 9th if she ovulated on that day. Shoe me every piece of scientific literature you're relying upon for that position sir, right now.

THE COURT: You want to take a recess?

THE WITNESS: Yes, sir. I'll be in my library.

BY MR. LOFTUS

Q Otherwise, I'm going to ask the Court to strike your answer because it is not, its not based on Daubert quality scientific evidence.

THE COURT: You asked his opinion and he gave his opinion.

THE WITNESS: Mr. Loftus, I'll be glad to provide you with names of references, work by Latero and Choy, Steven Gill. There's been a number of studies.

BY MR. LOFTUS

Q Just a minute. There's no question pending for you, Doctor, at this point.

THE COURT: He is explaining his answer.

MR. LOFTUS: What he could have done -- I believe he did not respond properly to my initial question. What I'm suggesting to Your Honor, with all due respect, is that under Daubert, a scientific opinion that he has just rendered must be stricken if it does not meet the quality requirement, and it's the responsibility of the defense to provide that.

This case has been pending for over three years. If they had scientific evidence that would support the theory that this penicillin taken for two days would not permit her, Karyn, to become pregnant, that should have been listed, listed and listed. If they don't produce it here, then we move the Court o strike.

THE COURT: That is cross examination, Counsel. His

answers are subject to cross examination.

MR. LOFTUS: Yes. But we move the Court to strike his answer.

THE COURT: I'll strike the question too then, right?

MR. LOFTUS: That's fine, Your Honor.

MS. KENNEY: Your Honor, we would object to that. Mr. Loftus has misplaced -- first of all, he asked the witness a question, he didn't like the answer, so he moves to strike it.

Then he says, "Do you have your library here so you can prove this to me," and of course the witness doesn't, but he won't let the witness give him references. Just because Mr. Loftus doesn't like the witness's answer isn't a good reason to strike the testimony.

MR. LOFTUS: That's the law I think, Your Honor, with all due respect.

THE COURT: Well, to the extent it's being used right here. In any event, if the answer goes out, so too does the question.

MR. LOFTUS: I don't believe he responded to the question.

THE COURT: Well, I've ruled, Counsel. Go on to our next subject.

MR. LOFTUS: Certainly. I didn't understand the Court had ruled.

THE COURT: Yes. (Tr. Vol 121395, 1246:17-1249:12)

More than Six months after the end of the trial the parties were still arguing the "Daubert hearing" to the Court during final arguments held on June 26, 1996, twit:

THE COURT: OKAY. NOW WE'VE BEEN QUITE AWHILE ON THIS SUBJECT. DO YOU WANT TO SWITCH TO THE QUESTION OF ANY STUDIES THAT SUPPORT THE HYPOTHESIS --

MR. LOFTUS: CERTAINLY.

THE COURT: -- THAT THE MEDICATION APPEARS AT ALL?

MR. LOFTUS: CERTAINLY.

THE COURT: I HAVEN'T FOUND ANY CONTROLLED STUDY THAT WOULD SO INDICATE.

MR. LOFTUS: I BEG YOUR PARDON?

THE COURT: I DON'T SEE ANY CONTROLLED STUDY THAT WOULD INDICATE THAT THIS HAS BEEN DEMONSTRATED SCIENTIFICALLY THAT THE MEDICATION DOES INTERFERE WITH THE PILLS. THERE'S A LOT OF HYPOTHESIS ABOUT IT AND ARGUMENT ABOUT IT, BUT DO YOU HAVE ANY CONTROLLED STUDIES THAT WOULD SUPPORT THAT OTHER THAN WHAT YOU'VE ALREADY CITED?

MR. LOFTUS: OTHER THAN WHAT?

THE COURT: OTHER THAN YOU'VE ALREADY CITED, OTHER THAN YOU ALREADY CITED IN THE TRIAL, ANY STUDIES?

MR. LOFTUS: WELL, I WOULD LIKE TO GO THROUGH THE STUDIES THAT I CITED IN MY PLAINTIFFS' PROPOSED FINDINGS OF FACT.

THE COURT: WERE THEY RELIED ON BY YOUR EXPERTS OR DID THEY COME TO DIFFERENT CONCLUSIONS?

MR. LOFTUS: THEY WERE RELIED ON BY BOTH THE PLAINTIFFS' EXPERTS, DOCTORS HINDERSTEIN AND HARRALSON, AND THREE OF THEM, THE --

THE COURT: THEY WERE CONTROLLED STUDIES BY TESTING?

MR. LOFTUS: EXACTLY.

THE COURT: ALL RIGHT.

MR. LOFTUS: EXACTLY. BACK '92.

MS. KENNEY: YOU MEAN '82?

MR. LOFTUS: BACK '82, I'M SORRY; SHENFIELD AND GRIFFIN STUDY AND THE SWENSON STUDY WERE ALL CITED BY DOCTORS HINDERSTEIN AND HARRALSON. THEY'RE REFERRED TO IN PLAINTIFFS' PROPOSED FINDINGS OF FACT BEGINNING ON PAGE 24.

THE FIRST ARTICLE CITED BY -- AND I MIGHT ADD, YOUR HONOR, THAT DR. ARCHER, WHO I THINK WAS HANDS DOWN THE BEST, MOST QUALIFIED AND, COMPARED TO THE OTHER DEFENSE EXPERTS, MOST CANDID IN HIS ANSWERS, DR. ARCHER AGREED THAT ALL THREE

OF THOSE ARTICLES I JUST REFERRED TO WERE SCIENTIFIC ARTICLES, GOOD SCIENCE ARTICLES BASED ON TESTS THAT INDICATED AN INTERACTION BETWEEN ANTIBIOTICS AND THE ESTROGEN COMPONENT OF ORAL CONTRACEPTIVES, AN ADVERSE INTERACTION. DR. ARCHER AGREED. (Tr. Vol. 62696, 56:13-58:5)

Cross-Examination of Dr. Archer by Mr. Loftus regarding Back '82:

Q In other words, if you've acknowledged that these statistics, the results of these tests do in fact show an interaction took place in the two women, and I suppose, depending upon the viewpoint that this author wanted to 09 get across to his reading public, he might have concentrated on those two women and said this test did in fact demonstrate that an interaction took place?

A I think he said that. (RT121295:1031) (Emphasis supplied)

Q Doctor, was this study conducted by Back, that is, the subject of this 1982 article, was that a test?

A Test?

Q Yes. I mean, a study and test in this sense are interchangeable words, are they not?

A Well, I don't use it that way, but if you want to use it that way, then it is a test, sir.

Q And if we turn back to page 44 of that Back article,

under Table 1, he sets out what you're supposed to do when you're conducting, essentially, a controlled test, does he not? He sets out the figures that he obtained as a result of his testing?

A Yes, he did does.

Q And referring to patient number one there under Table 1, that indicates that while that patient was on the antibiotic, ampicillin, she had an estrogen level of 60.3. But on the next go around where she was not on the ampicillin, that patient had an estrogen level of 88.7.

MS. KENNEY: I'm sorry. I'm going to object. It misstates the table. It's ethynyl estradiol.

MR. LOFTUS: It's EE.

Q That's what we're talking about, isn't it?

A EE, yes, sir.

Q Okay. Thank you. Is that not what that shows?

A Yes.

Q The results of that test?

A Um-hum. (Tr. Vol 121295, 1228:07-1229:08)

After reviewing the above Shenfield article for the first time the following testimony was elicited from Dr. Archer: Cross examination of Dr. Archer by Mr. Loftus 121295,1040:

13 Q The question is, does that material you just read
14 from the Shenfield and Griffin article, does that reflect a
15 test?
16 A A test?

17 Q Yes.
18 A Yes.
19 Q And does that test reflect that an interaction was
20 observed between the antibiotics and the EE level?
21 A It suggests that, yes.
22 THE COURT: Is that a scientific test?
23 THE WITNESS: It's scientific. The problem would
24 be helped if there Shenfield had followed it up with several
25 more cases to show that there is consistency, but there may be
1041

No valid claim can be made that Dr. Harralson attempted to "reinterpret the results" of Shenfield's controlled test, as this is exactly the result Shenfield noted in his report. Further, Back and Orme cited Shenfield in their 1994 report published in the Goldzieher booklet (Defendant's Exhibit 13.9), as evidence of the exact same interaction and result.

Swenson, Journal of Gastroenterology, 1990.

Once again Dr. Archer agreed that the Swenson study constituted a "test" (1024:12) and that the scientist conducting the test concluded that antibiotics interfered with some of the women's estrogen levels, towit:
Cross examination of Dr. Archer by Mr. Loftus:

1024:

13 Q Okay. And does that test suggest, as the authors
14 recommend at the bottom, that there was in fact an interaction
15 between the antibiotics and the estrogen levels as shown by that
16 test?
17 A I think the authors interpret this data as
18 indicating that the administration of the antibiotics reduce the
19 urinary excretion and increase the fecal excretion, yes.
20 Q So Doctor, would you say that that is in fact
21 scientific evidence of an interaction between antibiotics and
22 estrogen?
23 A Yes. (121295,1022:16-1024:9)

Excerpts from Rothman:

"The failure of some researchers to recognize the theoretical impossibility of "proving" the causal nature of an association has led to fruitless debates pitting skeptics who await such proof against scientists who are persuaded to make an inference on the basis of existing evidence.

The responsibility of scientists for making causal judgments was Hill's final emphasis in his discussion of causation:

All scientific work is incomplete--whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time. (Rothman, supra, Causal Inference in Epidemiology Plt's Ex. 160,p.20)

ONE EXAMPLE OF THE NEGATIVE INFLUENCE OF STATISTICAL THINKING IN EPIDEMIOLOGIC Practice is the dominance of statistical hypothesis testing in epidemiologic data analysis. The motivation for the development of statistical hypothesis testing was to provide a basis for decision making in agricultural and quality-control experiments....Ch1,p.4...

The notion of "statistical significance" could be expunged from the lexicon of the epidemiologist with no loss. Used to assess confounding, it is simply incorrect; used to test statistically the association between exposure and disease, it is

often misleading and never descriptive of the magnitude of effect or the precision of measurement. MODERN EPIDEMIOLOGY, by Kenneth J. Rothman, 1986, Boston, Little, Brown & Company, Ch9. THE ROLE OF STATISTICS IN EPIDEMIOLOGIC ANALYSIS, p.128.

Excerpts from deposition of Defendant's dental assistant Susan Balesteri taken on February 24, 1994:

q. Did you think there was something physically wrong with him or just psychologically or a combination or what?

a. Well, being high on drugs, well, that would be both physically and mentally, yes.

q. That was your impression at the time?

a. Yes.

0034

Q. Did you ever find out what drug he was taking?

a. I think that they found that he was using cocaine.

q. Did he ever confess this to you?

a. No.

q. Did they find out for what period of time he had been Using it?

a. Not that I know of.

q. How long had he been at your unit?

a. He came to the clinic in either late -- I think it was late 1988. Then he left for a few months the end of 1990 to go to -- end of '90, beginning of '91 he went to saudi arabia.

q. For --

a. For desert storm, right. And then he came back in may of '91, I think. He wasn't there -- he was only gone about six months.

q. And so did you notice anything different about him when he came back from saudi arabia?

19 a. Actually, no, not right away. He always -- even when
20 he first came he always was kind of a really hyper
21 wound-up personality. Other people who would see him
22 would often say things like, "god, is he always like
23 that?" We would just shrug and say, "yeah." Because
24 he was. He started out hyper and we just thought
25 that was the way his personality was.
26 q. But now you think there was something else?
0035
1 A. I think he may have actually had a problem all along.
2 q. With the drugs?
3 a. Right.
4 q. Did you have to stop him from making mistakes?
5 a. No. But the last six or eight months when it became
6 Apparent that he really seemed to have a problem, I
7 Was not working with him as much. I mostly was
8 Working with dr. caples.
9 q. Who was working with him?
10 a. Fran petruzzi.
11 q. Is she still out there?
12 a. No.
13 q. How do you spell her last name?
14 a. P-e-t-r-u-z-z-i.
15 q. Do you know where she is at now?
16 a. She lives in pacific grove.

Excerpt from pre-trial hearing on November 8, 1995:

Mr. Loftus: both the dental hygienist that Assisted the defendant's doctor on the day that he Prescribed -- ordered my client to take the pen vk Without warning her, will testify they thought he was On cocaine at the time.

the court: they thought he was on cocaine at the time?

mr. loftus: yeah, because -- and they will indicate why, because he was carrying the vials around and had the white stuff on his face and was acting crazy and that the army undertook an investigation and agreed with their suspicion.

that's their testimony. I mean, it's the employees of the defendants, not my witnesses.

ms. Kenney: the deposition testimony of ms. Balestreri does not come close to the representation just made by mr. loftus.

the court: this is fran -- is it fran?

mr. loftus: petruzzi, your honor, p-e --

the court: she's the one that's going to testify about the cocaine?

mr. loftus: both petruzzi and balestreri,

0037

Your honor. As a matter of fact defense, has the Deposition of balestreri where she expressed the same Sentiments.

the court: okay.

Summary of Ultrasound evidence:

April 30 Ultrasound:

HC (Hadlock) 14W 3DAYS 7X14=98+3=101DAYS

JAN27	5
FEB	29
MARCH	31
APRIL	30

TOTAL 95+6(or-6)= 101 (affirming LMP of Jan 27 & allowing for conception of February 9)

JUNE 10 Ultrasound:

CGA 19W2 7X19= 133+2=135 DAYS

JAN 27	4
FEB	29
MARCH	31
APRIL	30
MAY	31
JUNE	10

TOTAL 135DAYS (indicating LMP of Jan 27, Conception of Feb 9)

BPD 136DAYS

OCTOBER 6, 1992 ULTRASOUND REPORT OF DR. TIETELBAUM, SAYS CGA 36 WEEKS 1 DAY, GAVE BIRTH 11 DAYS LATER OR 37 WEEKS 5 DAY

37 x 7=259 + 5= 264 DAYS:

Jan27	**4**
Feb	**29**
March	**31**
April	**30**
May	**31**
June	**30**

July	**31**	
August	**31**	
Sept		**30**
Oct		**17**

Summary of Dr. Archer's Co-authored Study:

His study document follicular growth throughout the pill taking cycle in all three groups of 10 women subjects on oral contraceptives.See summary of Dr. Archer's study (D-13.6).

At page 3 of his study Dr. Archer proclaims at line 2: "The aim of this study was to determine the occurrence and functional capacity of ovarian follicular cysts (i.e. follicles) prospectively in normal fertile women using two triphasic (ethynyl estradiol with levonorgestrel or gestodene) and a low dose monophasic oral steroidal contraceptive (ethynyl estradiol and levonorgestrel). A control group consisted of women using a non-hormonal contraceptive. The contraceptive regimens were evaluated by imaging the ovaries with vaginal ultrasound on menstrual cycle days 1,6,11,16 and 21. Blood samples obtained at these times were analyzed for follicle stimulating hormone (FSH), estradiol-17B (E2) and progesterone (P).

At page 4, line 1: "Our results indicate that follicular development does occur in women using oral steroidal contraception..."

At page 5, line 1: "It appears that low dose oral contraceptive preparations do not result in complete suppression of ovarian function.....Forty (40) normally menstruating women between the ages of 18 and 35 years were asked to volunteer for the study...

RESULTS

At page 10, **SERUM FOLLICLE STIMULATING HORMONE**

Serum FSH levels on menstrual day one were comparable

in all four groups in all five observational cycles (see Fig. 1). [This finding dispels the red herring floated by defense counsel Kenney, Grimes, and Roy, that there is something different about the first day of the cycle of a woman on birth control pills, and a woman who is not. And explains why Dr. Archer did not object, as Dr. Grimes had to counting forward from Karyn's January 27 LMP.(Please compare Grimes at 1211:7 with Archer at 1059:22)

As determined by US, the Group A volunteers had no cyst >1.1 cm in any of the treatment cycles.[this is the only group that would support his above answers on direct.] **Two (2) of the ten (10) women in Group B had ovarian cysts >1.6cm with elevated P levels (3.0 ng/ml) during active treatment (Table 1). One woman (#49) in the second cycle (first treatment) and a second woman (#58) in all three treatment cycles; a third volunteer (#41) had cysts of 2.95 and 2.05 cm in two successive treatment cycles, but no increase in serum P levels (data not shown).**

On page 14 the report concludes:

"These data suggest that follicular development to an early antral stage may be occurred in women on oral steroidal contraception. It appears ovulation does not occur, but that atresia of these follicular cysts occurs. It is obvious that failure to take the subsequent oral contraceptives in a timely fashion could result in escape ovulation since serum FSH levels raise acutely after stopping oral estrogen."

Examination of Dr.Archer by Mr. Loftus:

21 Do you recall that statement?
22 A What is happening --
23 Q The question is if you recall?
24 A I recall.
25 Q Okay. And so likewise, if the effect of the oral

1082

01 contraceptive was interfered with not by not taking the oral
02 contraceptive as you have indicated there, but by an antibiotic
03 interfering with the oral contraceptive, there is no reason why
04 you shouldn't see the same phenomenon that you've just
indicated
05 and that ovulation could occur; correct?
06 A Theoretically that's possible, yes.

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Direct Examination of Dr. Jones by Ms. Kenney:

23 Q And does the FDA have a combination drug policy
24 which relates to this?
25 A Yes, they do. They require, in the combination
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01 policy, that when there are two components, each component of
a
02 combination drug must have its own independent effectiveness,
03 **and the combination must be effective by virtue of those two**
04 **components.** But each have to have their own contribution to
the
05 overall effectiveness.